THE JOURNAL OF GENERAL CHEMISTRY OF THE U.S.S.R.

Volume XXV, No. 1

January, 1955

(A Publication of the Academy of Sciences of the U.S.S.R.)

IN ENGLISH TRANSLATION

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CONSULTANTS BUREAU

152 West 42nd Street

New York 36, N.Y.

Printed in the United States

Annual subscription $ 95.00

Single issue 20.00

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QUATERNARY RECIPROCAL SYSTEMS OF THE CHLORIDES AND SULFATES OF LITHIUM, SODIUM AND POTASSIUM. I.

E. K. Akopov and A. G. Bergman

Our work on the investigation of the relationships existing in melts of the sulfates and chlorides of lithium, sodium and potassium showed that a more complex chemical activity exists among them than was assumed by earlier investigators.

The introduction of low-melting chlorides into melts of the sulfates of the same elements promotes the development of complex compounds and phase transformations.

The study yielded much interesting data on the problems of the formation and decomposition of solid solutions, on complex formation, and on the relationships of the shift of double decomposition reactions and complex formation [1, 2, 3].

The interaction between the sulfates of the elements specified seems to be rather complex, especially in the ternary systems [4, 5], in which two ternary sulfates form.

The sulfates and chlorides of lithium, sodium and potassium form complex quaternary reciprocal systems of the Li, Na, K‖Cl, SO_4 type in melts, the composition diagram of which is represented graphically in the form of a trihedral right-angled prism, in Fig. 1, where the positions of the salts are specified.

Quaternary systems, according to the phase rule, belong to the four-component systems. The overall process of the double decomposition reactions taking place in the complex systems mentioned above may be represented by the following equation:

$$Li_2SO_4 + Na_2SO_4 + 2K_2Cl_2 \longrightarrow 2K_2SO_4 + Li_2Cl_2 + Na_2Cl_2.$$

EXPERIMENTAL

From the prism of the reciprocal systems of Li, Na, K‖Cl, SO_4, we studied 12 profiles, which may be divided into three groups – diagonal, horizontal and volume profiles.

The investigation was carried out by the visual-polythermal method [1, 4]. The original salts of c.p. grade were carefully purified; and the melting points taken for the sulfates of lithium, sodium, and potassium were 856, 884, and 1069°, respectively, and for the chlorides of lithium, sodium and potassium they were 606, 800, and 774°, respectively. All compositions were expressed in molar percentages.

Diagonal Profiles

We studied 5 diagonal profiles. Of these, one profile, that of Na_2Cl_2–K_2Cl_2–Li_2SO_4, appeared to be stable [6], and the remaining ones were unstable

In three profiles, two belonging to these triangular sides appear as lateral diagonals of the reciprocal system prism, and the third appears as a lateral binary system – of the sulfates of the upper base of the prism. Thus, in each of these profiles, 2 sulfates and 1 chloride are the components.

The purpose of the study of these profiles was to make a determination of the orientation of the boundaries of the crystallization areas inside the prism, defining the lateral binary system of sulfates more accurately by adding a third component to the sulfate melt, in the present case – addition of a chloride.

Besides the profiles mentioned, we also studied non-diagonal profiles.

In the present article we analyze two profiles, the positions of which are shown in the composition prism in Fig. 1.

A. The Li_2SO_4–Na_2SO_4–K_2Cl_2 profile. The sides consist of: 1. Li_2SO_4–Na_2SO_4. Here are formed the two

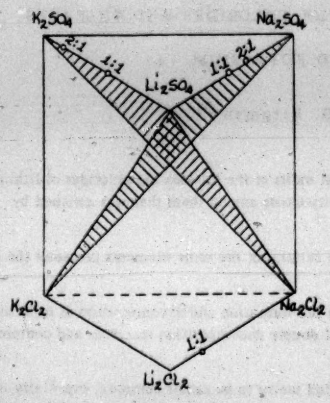

Fig. 1. Complex quaternary reciprocal system of Li, Na, K||Cl, SO_4. 1:1, 2:1, etc., of the corresponding binary compounds.

compounds, 1:1 and 1:2, which melt with decomposition at 620° and 637°. The fusion curves consist of four branches, which intersect at 637° and 62.5% Na_2SO_4, 620° and 48% Na_2SO_4, and 596° and 36.5% Na_2SO_4 [1].

2. K_2Cl_2–Li_2SO_4 – a stable diagonal profile of the reciprocal system, Li, K||Cl, SO_4, with a eutectic at 456° and 68% Li_2SO_4 [2].

3. K_2Cl_2–Na_2SO_4 – an unstable diagonal profile of the reciprocal system, Na, K||Cl, SO_4, which consists of three branches intersecting at 624° and 24.5% K_2Cl_2, and 525° and 41.5% K_2Cl_2 [3].

Internal profiles. We studied 14 internal profiles, the curves of which are presented in Fig. 2, and the general characteristics of which are given in the composite Table 1.

In Fig. 3, the crystallization surface diagrams of the given profiles are projected onto a triangular composition diagram: the isotherms were taken at 50° intervals, and for one of the isotherms, specified by the dotted line, at 25° intervals.

By means of the orthogonal projection of the crystallization onto the Li_2SO_4–Na_2SO_4 side (Fig. 4), the triple point is specified by position 8 in the triangle.

This represents its monovariant triple point, since the present system appears as a profile of the four-component reciprocal system studied; therefore, at the junction point, where three monovariant curves of joint crystallization intersect, one finds in equilibrium, not 4 phases, but 3.

The nature of these monovariant points is set forth in Table 2.

The surface diagram of the profiles studied consists of 9 areas of crystallization, and of this number, there are 2 areas of heteromorphic profiles of Li_2SO_4 having a transition point at 572°.

The isotherms in the KCl, Na_2SO_4 and [X] areas proceed smoothly; in the α-Li_2SO_4 area they lie crowded close together, whereas in the β-Li_2SO_4 area they are spaced at rather large distances from each other. In the Li_2SO_4·Na_2SO_4 area, the isotherms originate from the small part of the monovariant crystallization curve, of [Li_2SO_4]I[D_1] and elongate appreciably at the places of their intersection with the monovariant curve [D_1][D_2].

The upper limit of the temperature at which the internal phases can exist, designated by the letter [T], equals 476°, agreeing with the projection of the present crystallization profiles (Fig. 4); therefore, there is a basis for assuming that phase [T] should appear as a binary compound of the sulfates of sodium and potassium, with a 1:1 composition. The latter develops into a binary system, Na_2SO_4–K_2SO_4, as a result of the decomposition at 476° of the solid solutions of (Na, K)$_2SO_4$, the components of which form solid solutions to a limited extent. Phase [T] also appears in the two horizontal profiles of the prism.

We established the area of crystallization of NaCl from the external form of the crystals and from the general configuration of the quaternary reciprocal system. The crystallization area, [X], appears as an internal phase of reciprocal systems of Na, K||Cl, SO_4 [3].

B. The Li_2SO_4–K_2SO_4–Na_2Cl_2 profile. 1. Li_2SO_4–K_2SO_4 – forms clearly expressed compounds of 1:1 composition, melting without decomposition, and less distinctly expressed 2:1 compounds, melting with decomposition.

There is a heteromorphic point of transformation of Li_2SO_4 at 572° and 87% Li_2SO_4, a eutectic point at 532° and 81% Li_2SO_4 and 712° and 39.5% Li_2SO_4; there is a transition point at 550° and 76.5% Li_2SO_4, and a maximum at 732° and 50% Li_2SO_4 [2].

2. Na_2Cl_2–Li_2SO_4 – a stable diagonal profile of the reciprocal system, Li, Na||Cl, SO_4 [1], a eutectic system with a eutectic at 499° and 74% Li_2SO_4.

TABLE 1

No. of section	Original mixture of components (in %)	Added component	Branches of the crystallization curves and their intersections. Branch 1	Intersection of 1 and 2 % *	Intersection of 1 and 2 t°	Branch 2	Intersection of 2 and 3 %	Intersection of 2 and 3 t°	Branch 3	Intersection of 3 and 4 %	Intersection of 3 and 4 t°	Branch 4	Intersection of 4 and 5 %	Intersection of 4 and 5 t°	Branch 5
I	80 Li_2SO_4 + 20Na_2SO_4	KCl	α-Li_2SO_4	3.0	572	β-Li_2SO_4	18.5	462	[T]	27.0	452	KCl			
II	65 " + 35 "	"	"	4.0	482	$Li_2SO_4 \cdot Na_2SO_4$	13.0	462	"	23.0	446	"			
III	50 " + 50 "	"	$Li_2SO_4 \cdot 2Na_2SO_4$	15.5	458	NaCl	28.5	480	KCl						
IV	42 " + 58 "	"	"	16.0	462	"	30.0	492	"						
V	35 " + 65 "	"	Na_2SO_4	8.0	519	$Li_2SO_4 \cdot 2Na_2SO_4$	16.0	466	NaCl	31.0	495	KCl			
VI	20 " + 80 "	"	"	12.0	604	[X]	24.0	495	"	32.0	488	"			
VII	10 " "	"	"	17.0	628	"	34.0	497	KCl						
VIII	90 " + 10 K_2Cl_2	Na_2SO_4	β-Li_2SO_4	28.0	473	[T]	31.5	473	$Li_2SO_4 \cdot Na_2SO_4$	43.0	500	Na_2SO_4	61.0	582	Na_2SO_4
IX	82 " + 18 "	"	"	19.0	472	"	30.5	462	"	41.5	476	"	58.0	524	"
X	73 " + 27 "	"	"	12.0	455	"	30.0	451	NaCl	42.5	464	$Li_2SO_4 \cdot 2Na_2SO_4$	58.0	500	Na_2SO_4
XI	60 " + 40 "	"	KCl	29.0	466	NaCl	51.5	465	[X]						
XII	50 " + 50 "	"	"	40.0	480	"	57.5	478	"						
XIII	57 " + 43 "	"	"	30.0	470	"	49.0	446	[T]	63.5	464	β-Li_2SO_4			
XIV	58 " + 42 Na_2SO_4	KCl	$Li_2SO_4 \cdot Na_2SO_4$	16.0	451	"	28.0	464	KCl						

* % of added component.

TABLE 3

No. of section	Original mixture of components (in %)	Added component	Branches of the crystallization curves and their intersections. Branch 1	Intersection of 1 and 2 %	Intersection of 1 and 2 t°	Branch 2	Intersection of 2 and 3 %	Intersection of 2 and 3 t°	Branch 3	Intersection of 3 and 4 %	Intersection of 3 and 4 t°	Branch 4	Intersection of 4 and 5 %	Intersection of 4 and 5 t°	Branch 5
I	25 Li_2SO_4 + 75 K_2SO_4	NaCl	K_2SO_4	27	528	KCl	51.5	548	NaCl						
II	30 " + 70 "	"	"	23.5	522	"	48.5	538	"						
III	40 " + 60 "	"	α-D *	12.0	622	β-D	27.0	511	KCl	45	523	NaCl			
IV	50 " + 50 "	"	"	12	610	"	26.0	496	"	40.5	508	"			
V	62.5 " + 37.5 "	"	"	12	570	"	25.0	455	"	24.5	469	"			
VI	75 " + 25 "	"	L *	22	432	KCl									
VII	90 " + 10 "	"	α-Li_2SO_4	2.5	572	β-Li_2SO_4	24.5	464	KCl						
VIII	50 K_2SO_4 + 50 Na_2Cl_2	Li_2SO_4	KCl	52.0	444	L	65.0	463	β-Li_2SO_4						
IX	25 Li_2SO_4 + 75 "	K_2SO_4	NaCl	36.0	538	KCl	37.5	552	K_2SO_4						
X	50 " + 50 "	"	"	31.0	492	"	49	520	D	55.0	538	K_2SO_4			
XI	60 " + 40 "	"	"	26.0	467	"	37	486	"	57.5	568	"			
XII	75 " + 25 "	"	β-Li_2SO_4	17.0	442	L	25	460	"	59.0	627	"			
XIII	85 " + 15 "	"	"	18	464	D	26.0	484	"	61.5	661	"			
XIV	92 " + 8 "	"	α-Li_2SO_4	2.5	572	β-Li_2SO_4	18.95	510	L	25.0	678	D	61.5	678	K_2SO_4

* D = $Li_2SO_4 \cdot K_2SO_4$, L = $2Li_2SO_4 \cdot K_2SO_4$.

TABLE 2

Name of point	t°	Composition (in %)					Equilibrium phases
q_1	457	27.5	K_2Cl_2	63.5	Li_2SO_4	9 Na_2SO_4	Li_2SO_4, KCl, [T] •
q_2	476	5.0	"	63.0	"	32 "	Li_2SO_4, D_1, •[T] •
q_3	444	17.5	"	52.5	"	30 "	NaCl, D_1 [T]
q_4	452	23.0	"	48.5	"	28.5 "	NaCl, KCl, [T]
q_5	454	30.5	"	47.0	"	32.5 "	NaCl, D_1, D_2
q_6	538	7.0	"	33.0	"	60.0 "	Na_2SO_4, [X], D_2
q_7	464	15.5	"	29.0	"	55.5 "	[X], NaCl, D_2
q_8	492	32.5	"	8.5	"	59.0 "	NaCl, KCl, [X]

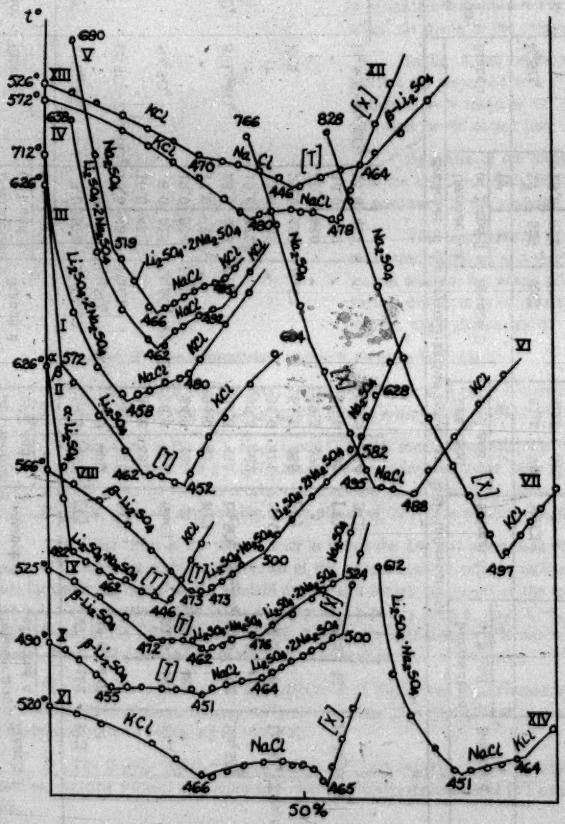

Fig. 2. Internal profiles through the first profile of $Li_2SO_4-Na_2SO_4-K_2Cl_2$.

• $D_1 = Li_2SO_4 \cdot Na_2SO_4$. $D_2 = Li_2SO_4 \cdot 2Na_2SO_4$. $[T] = Na_2SO_4 \cdot K_2SO_4$.

3. $Na_2Cl_2-K_2SO_4$ — an unstable diagonal profile of the reciprocal system, Na, K||Cl, SO_4, consisting of 3 branches intersecting at 554° and 57% K_2SO_4, and 568° and 41.5% K_2SO_4 [3].

Internal profiles. We studied 14 internal profiles, the curves of which are represented in Figs. 5 and 6, and the general characteristics of which are given in the composite Table 3.

Profiles XII, XIII, and XIV pass near the $Li_2SO_4-K_2SO_4$ side. A small part of the branch of crystallization on curves of these profiles indicates the presence of a new phase, which should come from the binary system, $Li_2SO_4-K_2SO_4$. We studied this system in detail and found a small branch, rather insignificantly expressed on the diagram, of $Li_2SO_4-K_2SO_4$ (4 mole % on the composition axis), and its presence could be considered doubtful, but its existence confirms sections XII, XIII and XIV.

In our opinion, this branch corresponds to the 2:1 compound, ($2Li_2SO_4 \cdot K_2SO_4$), which melts with decomposition at a temperature of 550°; therefore, it is feasible to call it lithium langbeinite. It should be pointed out that the presence of NaCl in the melt of the sulfates of lithium and potassium appreciably promotes the appearance of the specified compounds, which is quite evident both from the curves of the sections, and from the phase changes during the transition from the 2:1 compound to the 1:1 phase. With the aid of the present profiles, we succeeded in confirming the formation of the compounds indicated.

In Fig. 7, a complete projection of the diagrams onto a

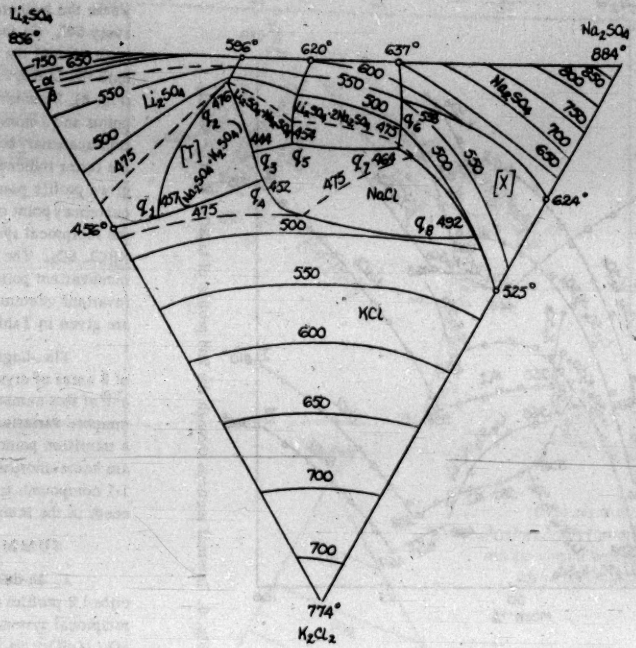

Fig. 3. Projection of the crystallization surface of the first profile of $Li_2SO_4-Na_2SO_4-K_2Cl_2$ onto a triangular basis.

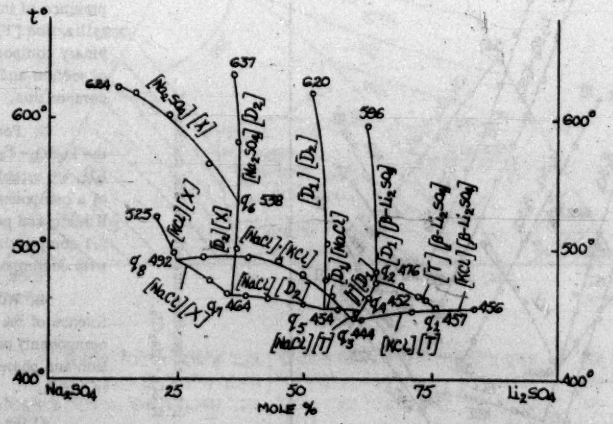

Fig. 4. Projection of the crystallization onto the $Li_2SO_4-Na_2SO_4$ side. Explanation in the text and in Table 2.

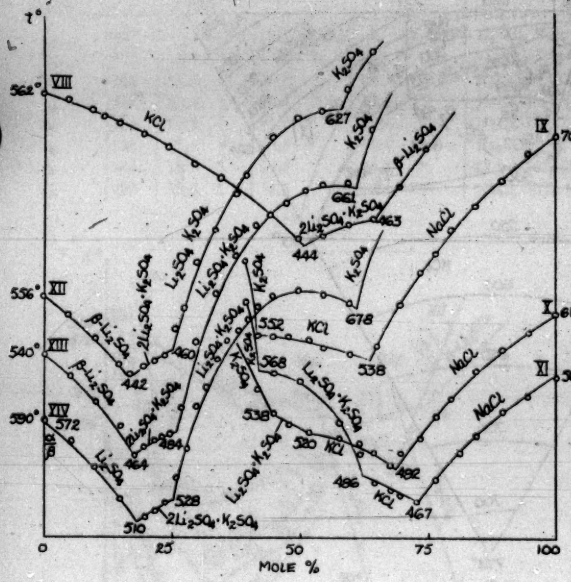

Fig. 6. Internal sections through the 2nd profile of $Li_2SO_4-K_2SO_4-Na_2Cl_2$.

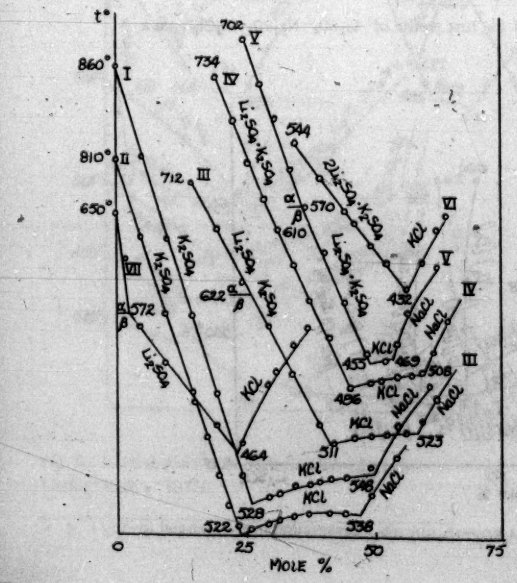

Fig. 5. Internal profiles through the 2nd section of $Li_2SO_4-K_2SO_4-Na_2Cl_2$.

composition triangle is presented where the isotherms were taken every 50°. On the basis of the projection of the crystallization onto the $Li_2SO_4-K_2SO_4$ side (Fig. 8), 2 monovariant ternary points and 1 nonvariant transition quaternary point appeared; the latter indicated that the given profile passes close to the quaternary point of the prism of the reciprocal system, Li, Na, K‖Cl, SO_4. The natures of these monovariant points (q) and the invariant quaternary point (p) are given in Table 4.

The diagram consists of 8 areas of crystallization, and of this number, 2 are heteromorphic varieties of Li_2SO_4 with a transition point of 572°, and 2 are homeomorphic forms of the 1:1 compound; transition proceeds in the interval 525-625°.

SUMMARY

1. In this report we described 2 profiles of the quaternary reciprocal system, Li, Na, K‖Cl, SO_4: $Li_2SO_4-Na_2SO_4-K_2Cl_2$, which appear to be unstable profiles.

2. In the $Li_2SO_4-Na_2SO_4-K_2Cl_2$ profile, we established the presence of internal phase of crystallization [T], appearing as the binary compound of the sulfates of sodium and potassium of 1:1 composition.

3. For the first time, in the $Li_2SO_4-K_2SO_4-Na_2Cl_2$ profile, we established the formation of a compound of the sulfates of lithium and potassium having a 2:1 composition, and melting with decomposition at 550°.

4. We showed the influence of the medium (third component) on complex formation and phase transformation, in which:

a) the presence of sodium chloride in the sulfate melt favors the development of the

TABLE 4

Name of point	t°	Composition in %	Equilibrium phases
p	436	24.0 NaCl; 51.0 Li_2SO_4; 25.0 K_2SO_4	KCl, NaCl, $Li_2SO_4 \cdot K_2SO_4$, $2Li_2SO_4 \cdot K_2SO_4$
q_1	428	21.5 NaCl; 61.0 Li_2SO_4; 17.5 K_2SO_4	NaCl, Li_2SO_4, $2Li_2SO_4 \cdot K_2SO_4$
q_2	522	24.5 NaCl; 22.5 Li_2SO_4; 53.0 K_2SO_4	KCl, K_2SO_4, $Li_2SO_4 \cdot K_2SO_4$

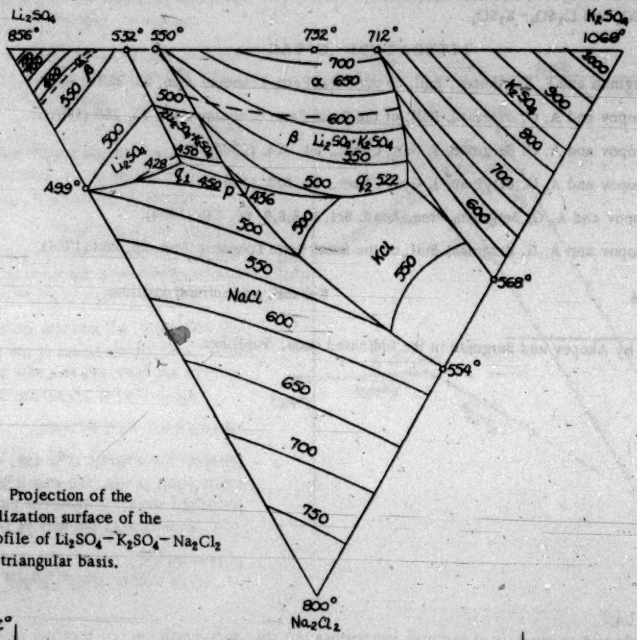

Fig. 7. Projection of the crystallization surface of the 2nd profile of $Li_2SO_4-K_2SO_4-Na_2Cl_2$ onto a triangular basis.

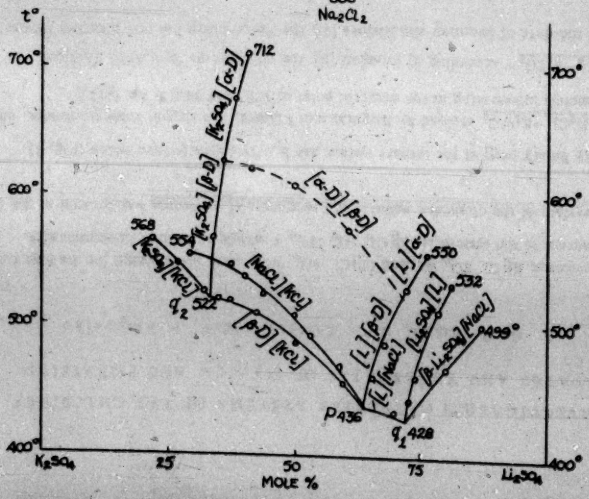

Fig. 8. Projection of the crystallization onto the $Li_2SO_4-K_2SO_4$ side. Elucidation in the text and in Table 4.

compound, $2Li_2SO_4 \cdot K_2SO_4$, but has a less favorable influence on the occurrence of transformation of the type II compound, $Li_2SO_4 \cdot K_2SO_4$;

b) potassium chloride favorably influences the development of the compounds, $Li_2SO_4 \cdot Na_2SO_4$ and $Li_2SO_4 \cdot 2Na_2SO_4$.

5. Quadruple transition points developed at 436° and 24% of Na_2Cl_2, 51% Li_2SO_4, 25% K_2SO_4 (the $Li_2SO_4 - K_2SO_4 - Na_2Cl_2$ profile of the quaternary reciprocal system, Li, Na, K‖Cl, SO_4).

6. During the investigation of the profiles mentioned, we specified the fusion curves of the binary systems: $Li_2SO_4 - Na_2SO_4$ and $Li_2SO_4 - K_2SO_4$.

LITERATURE CITED

[1] A. G Bergman and E. K. Akopov, Bull. of the Rural Farm Economy Assn. 23, 222 (1953).

[2] E. K. Akopov and A. G. Bergman, Bull. of the Rural Farm Economy Assn. 25, 255 (1954).

[3] E K. Akopov and A. G. Bergman, J. Gen. Chem., 24, 524, (1954). •

[4] E. K. Akopov and A. G. Bergman, J. Gen. Chem., 24, 512, (1954). •

[5] E. K Akopov and A. G. Bergman, Proc. Acad. Sci. U.S.S.R. 96, 523 (1954).

[6] E. K. Akopov and A. G. Bergman, Bull. of the Rural Farm Economy Assn. 25, 263 (1954).

Received July 19, 1954

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• There are no papers by Akopov and Bergman in the indicated issue. Publisher.

INVESTIGATION OF TERNARY SYSTEMS OF THE CHLORIDES, SULFATES AND TUNGSTATES OF LITHIUM AND POTASSIUM. II.

A. G. Bergman, A I. Kislova and V. I. Posypaiko

The ternary systems, K‖Cl, SO_4, WO_4 and Li‖Cl, SO_4, WO_4, were investigated for the first time. They appear in the prism diagram of the system, Li, K‖Cl, SO_4, WO_4, • which we studied fundamentally.

The ternary system of the chlorides, sulfates and tungstates of potassium was located at the lower base of the prism.

The secondary binary parts of the ternary system are briefly characterized below (Fig. 1).

The system K_2Cl_2–K_2WO_4, studied by Bergman and Kislova, is a simple eutectic system, consisting of the K_2WO_4 and K_2Cl_2 branches intersecting at the eutectic point at 618° and 44.5 % K_2Cl_2 [1].

System K_2WO_4–K_2SO_4 – according to Amadori [2], the components form solid solutions.

According to the data of Bergman and Kislova [1], the fusion curve has two branches intersecting at 916° and 35% K_2SO_4.

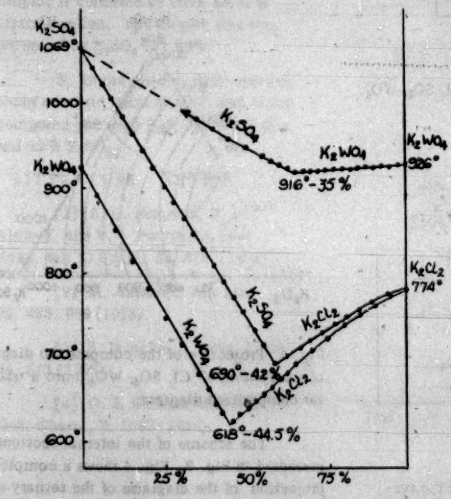

Fig. 1. Binary parts of the ternary system, K‖Cl, SO_4, WO_4.

The system K_2Cl_2–K_2SO_4 was first studied by E. Jänecke [3].

According to the data of Dombrovskaya [4], the K_2SO_4 and K_2Cl_2 branches intersect at the eutectic point at 690° and 42% K_2SO_4 (according to Jänecke, the eutectic is at 698° and 43% K_2SO_4).

INTERNAL SECTIONS

The results of the studies of the six internal sections are presented in Table 2. And in Fig. 2, the crystallization curves of the internal sections are presented. We describe them briefly.

Section 1. 57.5 % K_2Cl_2 + 42.5% K_2SO_4 → → K_2WO_4 intersects the areas of: K_2Cl_2, K_2SO_4, and K_2WO_4 corresponding to 678° and 5% K_2WO_4 and 678° and 45% K_2WO_4.

Section 2: 55% K_2WO_4 + 45% K_2Cl_2 → → K_2SO_4 intersects the areas of: K_2Cl_2, K_2WO_4, K_2SO_4 at 610° and 6% K_2SO_4, and 644° and 18% K_2SO_4.

Section 3: 50% K_2WO_4 + 50% K_2SO_4 → → K_2Cl_2 proceeds through the areas of K_2SO_4 and K_2Cl_2 at 620° and 50% K_2Cl_2.

Section 4. 75% K_2Cl_2 + 25% K_2WO_4 → → K_2SO_4 intersects the area of K_2Cl_2 and K_2SO_4 at 650° and 31% K_2SO_4.

Section 5: 80% K_2WO_4 + 20% K_2SO_4 → → K_2Cl_2 proceeds through the areas of K_2WO_4 and K_2Cl_2 at 600° and 45% K_2Cl_2.

• The investigations were carried out by the visual-polythermal method.

Section 6: 80% K_2WO_4 + 20% K_2Cl_2 ⟶ K_2SO_4 proceeds through the areas of K_2WO_4 and K_2SO_4 at 816° and 30% K_2SO_4.

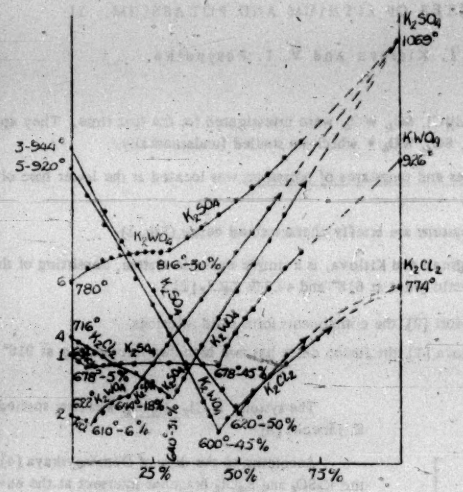

Fig. 2. Internal sections of the ternary system, K | Cl, SO_4, WO_4.

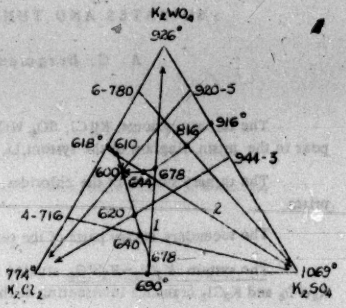

Fig. 3. Direction of the internal sections of the ternary system, K | Cl, SO_4, WO_4.

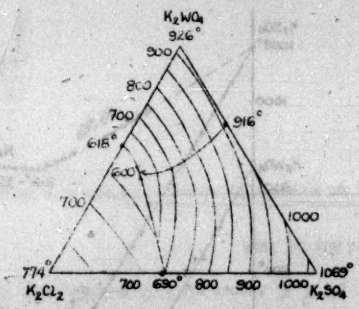

Fig. 4. Projection of the composition diagram of the system, K | Cl, SO_4, WO_4, onto a triangular composition diagram.

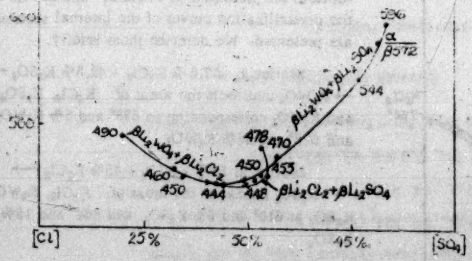

Fig. 5. Projection of the joint crystallization lines of the ternary system, K | Cl, SO_4, WO_4, onto the K_2Cl_2–K_2SO_4 side.

The scheme of the internal sections is presented in Fig. 3. Fig. 4 shows a complete projection of the diagrams of the ternary systems investigated, onto a equilateral triangular composition diagram; the isotherms were taken at every 50°. A projection of the crystallization areas of the triangular composition diagram onto the K_2Cl_2–K_2SO_4 side is shown in Fig. 5.

The diagram of the crystallization surfaces of the system consists of the three areas of crystallization.

The sizes of the areas, expressed as percentages of the total area of the triangle, amounted to: potassium chloride, 26.23; potassium tungstate, 22.54; and potassium sulfate, 51.23 %.

TABLE 1

Secondary Binary Systems

$K_2Cl_2-K_2WO_4$		$K_2WO_4-K_2SO_4$		$K_2Cl_2-K_2SO_4$	
% K_2Cl_2	t°*	% K_2SO_4	t°	% K_2Cl_2	t°
0	926	0	926	0	1069
5	874	2.5	924	3	1044
10	850	5	922	6	1026
15	812	7.5	922	9	1010
20	780	10	922	12	986
25	746	12.5	922	15	970
30	712	15	920	18	948
35	678	17.5	920	21	924
37	664	20	920	24.5	902
40	642	22.5	918	27.5	884
42	632	25	918	30.5	866
45	622	27.5	916	33.0	848
47	628	30	916	36.5	828
50	638	32.5	916	39.5	808
52	642	35	916	42.5	790
55	652	37.5	920	45.5	770
57	660	40	924	48.5	754
60	672	42.5	928	51.5	732
62	678	45	934	54.5	713
65	686	50	944	57.5	692
70	704	55	956	62.0	698
75	716	60	968	66.0	706
80	734	65	980	69.5	713
85	744	100	1069	73.0	724
90	754	+	—	77.0	734
95	766	—	—	81.0	740
100	774	—	—	85.0	750
—	—	—	—	89.0	760
—	—	—	—	94.5	770
—	—	—	—	100	774

* Equimolar per cents of added component.

** Melting temperatures.

TABLE 2

Internal

Section 1		Section 2		Section 3		Section 4		Section 5		Section 6	
%K_2WO_4	t°	%K_2SO_4	t°	%K_2Cl_2	t°	%K_2SO_4	t°	%K_2Cl_2	t°	% K_2SO_4	t°
0	694	0	622	0	944	0	716	0	920	0	780
2.5	685	2.5	618	5	900	2.5	710	5	884	5	796
5	678	5	615	10	864	5	704	10	850	10	808
7.5	678	7.5	615	15	828	7.5	695	15	840	12.5	808
10	678	10	625	20	800	10	690	20	785	15	810
12.5	678	12.5	636	25	770	15	680	25	750	17.5	810
15	680	15	644	30	738	20	672	30	718	20	812
20	682	17.5	644	35	710	25	660	35	678	25	816
25	682	20	656	40	678	27.5	652	40	638	30	816
30	682	22.5	666	45	650	30	644	42.5	618	32.5	825
35	682	25	678	50	620	32.5	650	45	600	35	834
40	680	30	704	55	644	35	664	47.5	618	40	846
45	678	35	734	60	665	40	704	50	632	45	860
47.5	704	40	760	65	690	45	738	55	650	50	880
50	718	45	790	70	706	50	770	60	666	55	896
52.5	735	50	815	—	55	—	800	65	678	60	910
55	748	55	840	—	60	—	828	70	695	65	930
60	770	60	866	—	—	—	—	75	710	70	950
65	795	—	—	—	—	—	—	—	—	—	—
70	815	—	—	—	—	—	—	—	—	—	—

SUMMARY

1. The ternary system, K‖Cl, SO_4, WO_4, was investigated by the fusion method.

2. The system was extremely simple; it consisted of three areas of crystallization. The largest area was occupied by K_2SO_4–51.23%.

3. In the system, there was one ternary eutectic point at 600°, and it was composed of: 44% K_2WO_4, 44% K_2Cl_2, and 12% K_2SO_4.

LITERATURE CITED

[1] A. G. Bergman, A. I. Kislova, and V. I Posypaiko, Proc. Acad. Sci. U.S.S.R., 88, 815, (1953).

[2] M. Amadori, Att. Linc. 22, 453, 609 (1913).

[3] E. Jänecke, Z. phys. Chem. 64, 343 (1908).

[4] O. S. Dombrovskaya, J. Gen. Chem., 3, 1007 (1953).

Received April 19, 1954

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THE SOLUBILITIES OF LITHIUM AND POTASSIUM SULFATES IN WATER AT 25°. II

A. P. Yanko and I. G. Druzhinin

Lithium and potassium sulfates have great theoretical value and seem to be very important practically also. In connection with practical demands, at present there is a growing interest in the production of chemically pure lithium salts, which are obtained from minerals by conversion of the lithium to its soluble sulfate or chloride salts. Therefore, the equilibrium conditions and methods of separating lithium sulfate from the corresponding potassium and sodium salts present a most important problem, and require a detailed polythermal study of the aqueous system containing these salts. The ternary system of lithium and potassium sulfates and water has not been studied thoroughly.

In the old reports of Vyrubov [1], Vulf [2], Scacchi [3], Rammelsberg [4], Traube [5], Nacken [6], Schabus [7] and others it was observed that lithium sulfate might form chemical compounds of the double salt type with potassium sulfate. However, the opinions of these investigators were very contradictory concerning the establishment of the chemical composition of the double salt. For example, to one of the double salts, the following compositions were given: $Li_2SO_4 \cdot K_2SO_4$, $2Li_2SO_4 \cdot K_2SO_4$, and $Li_2K_4(SO_4)_5 \cdot 5H_2O$, etc. The purely practical requirements connected with the treatment of lithium-containing minerals and the isolation of pure lithium salts served as a stimulus to investigate the system Li_2SO_4–K_2SO_4–H_2O, again; the system was studied earlier by Spielrein [8] at 20, 60 and 98°. In his research, Spielrein confirmed the old data of other investigators, and attempted to demonstrate the existence of only one double salt having the molecular ratio, K: Li=1: 1. But since the results of Spielrein's studies were incomplete and included ambiguities, his data were somewhat doubtful. Spielrein obtained data only for compositions of solutions at the junction points, where instead of the expected salting out of lithium sulfate by potassium sulfate, there was an increase of the solubility of the former. For chemical analysis of the solutions corresponding to the transition points, Spielrein determined lithium by the Carnot method, which is based on the precipitation of lithium fluoride. This method has now lost its value to analytical chemistry, because of the relatively large solubility of lithium fluoride (100 ml of water dissolves 270 mg of lithium fluoride). He did not determine the potassium content, but calculated it by difference. No analysis of the solid phase was made; the conclusion concerning the separation of the double salt was made on the basis of graphical data and microscopic observations.

Because of the outstanding importance of systems of lithium and potassium sulfates and water, we decided to fill the existing gaps of knowledge, and to study the solubility isotherm of this sytem at 25°, for which data are entirely lacking in the literature.

EXPERIMENTAL

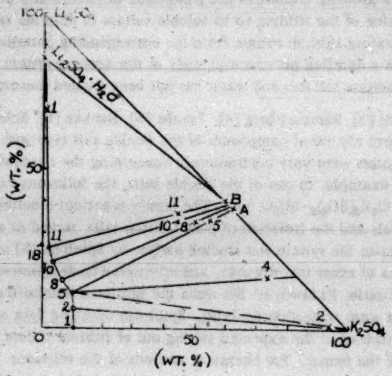
Investigation of the system was carried out in a water thermostat. The moment of attainment of equilibrium was determined by a series of chemical analyses, which were repeated throughout 5-8 hours until the data for the final samples agreed. Lithium was determined by the periodate method, potassium in the form of the cobaltinitrite, and sulfate-ion as $BaSO_4$. The uniformity of the solid phase was controlled by microscope, before the selection of each sample.

The solubility isotherm of lithium and potassium sulfates at 25° has three branches. The first branch, from point 1 to 5, corresponds to the crystallization of sulfate. The straight line connecting the diagram point of the solution and dry residue converges at the potassium sulfate terminal, indicating a 10% content of this salt in the solid phase. Point 5 appears to be a transition point, and corresponds to a solution having the following chemical composition: lithium sulfate, 10.76% and potassium sulfate, 10.46%. In agreement with the data of the physico-chemical diagram and chemical analysis, point 5 of the solid phase corresponds to the composition of the original components in a ratio of K: Li = 1: 1. In other words, under these conditions, a double chemical compound, $Li_2SO_4 \cdot K_2SO_4$, crystallizing in the form of individuals of hexagonal syngony, separates in the solid phase from solutions of the given composition. The middle branches from point 5 to 11 correspond to separations of double salts in isomorphic mixture with lithium sulfate (points A and B). The straight line connecting the diagram point of solutions and dry residues at the composition line of the actual solid phase takes the shape of a fan, indicating the formation of a single solid solution, developed on the lithium sulfate side.

The limiting ratio of K: Li in the solid solutions fluctuates from 1: 1 to 1: 1.08. Points 11-15 seem to be

Solubility of the System, Lithium Sulfate–Potassium Sulfate–Water at 25° C

Expt. No.	Composition of the liquid phase (in %)				Composition of the precipitate (in wt. %)				Solid phase
	Li_2SO_4	K_2SO_4	Σ-salt	H_2O	Li_2SO_4	K_2SO_4	Σ-salt	H_2O	
1	–	10.77	10.77	89.28	–	100	100	–	K_2SO_4
5	10.76	10.46	21.22	78.78	30.32	54.39	84.71	15.29	$Li_2SO_4 \cdot K_2SO_4$
7	13.05	8.09	21.14	78.86	31.35	45.99	77.33	22.67	Solid solution
10	20.93	3.25	24.18	75.82	35.05	45.95	81.00	19.00	Solid solution
16	25.85	1.03	26.88	73.12	66.20	0.69	66.89	33.11	$Li_2SO_4 \cdot H_2O$



Solubility isotherms of the system, $Li_2SO_4–K_2SO_4–H_2O$ at 25°

transition points and have, on the average, the following salt composition: lithium sulfate, 25.85% and potassium sulfate, 2.31%. This solution composition remains constant up to the diagram point of the actual solid phase determining the straight line, and is not displaced from the limiting point B to the point of the monohydrate of lithium sulfate.

The solid phase, corresponding to the middle branches of the crystallization curve, separates as hexagonal crystals, which from solutions of 10.76% lithium sulfate, 10.46% potassium sulfate, and 78.78% of water, crystallize as a double salt in the form of hexahedral plates, with a K:Li = 1:1. Later, according to the degree of accumulation of lithium sulfate isomorphically entrained in the solid solution (with double salt), the crystals sharply change in form, being converted to bipyramids. The growth of the bipyramides on the surfaces of the hexagonal plates proceed irregularly, as a result of which monocrystals having different sizes of bipyramids form. H. Traube [5], studying the crystallo-optical properties of this double salt, observed that from acid media the crystals can separate in the form of a new, third form –hexagonal prisms.

The study that we made of the crystallo-optical properties showed that the double salt has the following constants: angle ρ 62° 40', indices of refraction, n_D 1.474, n_p 1.471, a:c = 1:1.675.

SUMMARY

1. For the first time, the system, lithium and potassium sulfate–water, was studied at 25°.

2. The solubility isotherm of this system at 25° was characterized by the presence of three crystallization branches, corresponding to the separation of anhydrous potassium sulfate, lithium sulfate monohydrate and solid solutions.

3. Solid solutions formed at the expense of isomorphic mixtures of double salts with lithium sulfate. The limits of the solid solutions fluctuated within the molecular ratios of K:Li = 1:1 to 1:1.08. The existence of a solid phase of variable composition for these substances was established for the first time.

4. The double salt $Li_2SO_4 \cdot K_2SO_4$ should be considered as a limiting case of the solid solutions, $mLi_2SO_4 \cdot nK_2SO_4$, separating from aqueous solutions of lithium and potassium salts.

5. These data, apart from their theoretical value, may be used under plant conditions for separation of the sulfate salts and for the isolation of pure lithium sulfate.

LITERATURE CITED

[1] P. Virubov, Bull. Soc. Min., 3, 198 (1880); 13, 224 (1893).

[2] G. Vulf, Z. Kryst. 17, 595 (1890); 21, 255 (1893).

[3] Scacchi, Atti Acad. Napoli, 27, 3, 98 (1866-68).

[4] C. Rammelsberg, Pogg. Annal., 66, 76 (1845); 128, 313 (1866).

[5] H. Traube, N. Jahrb. Min., 5, 59 (1892); 1, 177 (1894).

[6] R. Nacken, N. Jahrb. Min., 24, 46 (1907).

[7] J. Schabus, Bestimmung der Krystallgest. in chemischen Laboratorien erzeugter Producten, Wien, 15 (1855).

[8] C. Spielrein, Comptes rend., 155, 346 (1912); 157, 48 (1913).

Received July 14, 1954

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RATE OF DECOMPOSITION OF BF'_4 IN WATER-ETHANOL MIXTURES; SOLUBILITY OF SODIUM TETRAFLUOROBORATE IN WATER AND ALCOHOL

I. G. Ryss and V. A. Plit

As one of us found earlier [1], the decomposition of BF'_4 in alkaline solution, according to the stoichiometric equation,

$$BF'_4 + 4OH' = BO'_2 + 4F' + 2H_2O,$$

seems to be a slow reaction of the first order. The reaction rate is determined by the hydrolysis step

$$BF'_4 + H_2O = BF_3OH' + HF.$$

Berzelius showed [2] that on attempting to salt out $Ba(BF_4)_2$ from the aqueous solution by using alcohol, decomposition of the salt resulted. Proceeding from this, it may be assumed that the presence of alcohol sharply increases the rate of decomposition of BF'_4. In this case, in order to obtain pure tetrafluoroborate, it was not possible to use alcohol as the salting-out agent, or as a water-alcohol medium for recrystallization.

For the solubility of $NaBF_4$ in water, only approximate data are known [3]: 52% at 24° and 60% at 60°. Data on its solubility in alcohol and in water-alcohol mixtures is lacking.

EXPERIMENTAL

The rate of decomposition of BF'_4 in a solution of alkali in a 50% water-ethanol mixture. The sample of $NaBF_4$ that we used did not contain a qualitatively definite mixture (alkalinity, BF_3OH', F', Cl', SO''_4). The titrated solution of alkali was freed from its mixture with carbonate.

A weighed portion of $NaBF_4$ was introduced into a solution of alkali that had been weighed, and heated in a thermostat; samples of solution were removed periodically with a pipet, and titrated with a solution of acid from a microburet, or titrated with alkali after complete consumption of the alkali that was introduced into the original mixture. The weight of the volume of solution removed by pipet was determined by weighing part of the sample; the amount of $NaBF_4$ and NaOH in each sample was calculated from their original quantities, and the ratios and the weights of the samples and their solutions. For the remaining part of the method, the experiments and calculations carried out were no different from those described earlier [1].

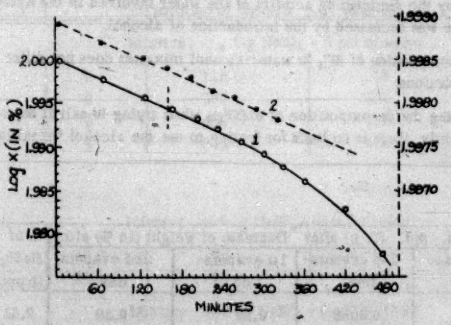

Fig. 1. 1) Decomposition of 0.09938 M solution of $NaBF_4$ in aqueous solution at 49.8° in relation to time (left ordinate); 2) decomposition of 0.1000 M solution of $NaBF_4$ in 50.6% water-ethanol mixture at 49.8° in relation to time (right ordinate).

For control, the rate of decomposition of BF'_4 in aqueous solutions, at a given temperature, was repeatedly determined.

Curve 1, Fig. 1 (left ordinate) illustrates the decomposition, with time, of the aqueous solution that was 0.09938 M with respect to $NaBF_4$ and 0.00563 M with respect to NaOH, at 49.8 ± 0.25°. At the time we selected the fourth sample the solution was acid, however, as also was observed earlier [1], the autocatalytic decomposition of BF'_4 is observed only after accumulation of sufficient acidity. The calculation of the mean rate constant value for the straight-line part of the graph, proceeds according to the equation

$$\log_{10} \frac{x_0}{x} = k'\theta,$$

where $\underline{x}$ is the percent of undecomposed BF'_4, θ is the time in minutes, equal to $3.58 \cdot 10^{-5}$ 1/min.; this agrees well with the quantity, $3.65 \cdot 10^{-5}$ 1/min., calculated according to [1].

Curve 2, Fig. 1 (right ordinate; the scale of the ordinate is increased by a factor of 10) represents the decomposition with time of the solution that was 0.10000 M in $NaBF_4$ and 0.00563 M in NaOH in a water-alcohol mixture (50.6 weight % of C_2H_5OH). In connection with the sluggishness of the reaction and the negligible change of the alkalinity of the solution with time, the points diverge more than in the former experiment. The average value of the rate constant, $\underline{k'} = 3.44 \cdot 10^{-6}$, i.e., it is smaller by a factor of 10.4 than it is in aqueous solution.

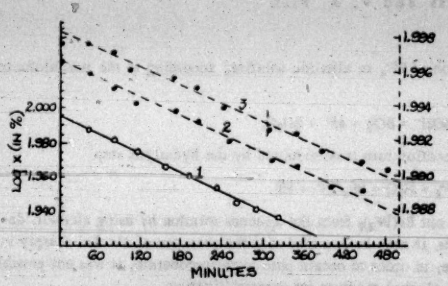

Fig. 2. 1) Decomposition of 0.01094 M solution of $NaBF_4$ in aqueous solution at 70° in relation to time (left ordinate); 2) decomposition of 0.0875 M solution of $NaBF_4$ in 50% water-ethanol mixture at 70° in relation to time (right ordinate); 3) the same for 0.1750 M solution of $NaBF_4$ (right ordinage).

Curve 1, Fig. 2 (left ordinate) represents the relation of log $\underline{x}$ to the time for an aqueous solution 0.01094 M in $NaBF_4$ and 0.00563 M in NaOH at 70 ± 0.10°. The average value, $\underline{k'} = 1.85 \cdot 10^{-4}$, agrees satisfactorily with that found earlier, $1.73 \cdot 10^{-4}$, at 69.95°.

Curves 2 and 3 of Fig. 2 (right ordinate; scale of the ordinate increased by a factor of 10) represent the decomposition of: a) 0.08750 M, and b) 0.17500 M solutions of $NaBF_4$ in water-alcohol mixtures (50 weight % C_2H_5OH). The original molarity for NaOH in both cases was equal to 0.01126. For experiment b), beginning with point θ = 309 minutes, the solution was acid, but the autocatalytic region did not appear at once. The average values were $\underline{k'} = 1.79 \cdot 10^{-5}$ and $1.76 \cdot 10^{-5}$, respectively, for experiments a) and b). Consequently, also at 70°, the decomposition of BF'_4 in water-alcohol solutions is smaller by a factor of approximately 10.4 than that in water solution.

From data on the partial pressures of the vapor from water alcohol mixtures [4], it resulted that in mixtures containing 50% alcohol, the activity of water was equal to 0.82 at 40° and 0.84 at 76°. Consequently, the sharp decrease of the reaction rate cannot be accounted for by the diminishing activity of the water involved in the hydrolysis process. The entropy of activation of the reaction was decreased by the introduction of alcohol.

The temperature coefficient of the rate of decomposition of BF'_4 in water-alcohol mixtures does not differ practically from that found earlier [1] for aqueous solutions.

Thus, the admonishment of Berzelius, concerning the decomposition of $Ba(BF_4)_2$ when trying to salt it out of aqueous solutions with alcohol, is erroneous. Apparently, there is no basis for fearing to use the alcohol for salting out and for recrystallization of the tetrafluoroborate.

TABLE 1

Expt. No.	Weighed portion of $NaBF_4$ (in g)	Solvent	Volume of solvent (in ml)	Weight of ppt. (in g) after 1st evaporation	Weight of ppt. (in g) after 2nd evaporation	Decrease of weight (in %) after 1st evaporation	Decrease of weight (in %) after 2nd evaporation	% of $NaBF_3OH$ in ppt.
1	0.2040	Water	1	0.2034	0.2032	0.29	0.39	2.61
2	0.2002	Water*	1	0.2000	0.2000	0.10	0.10	0.34
3	0.0798	C_2H_5OH	5	0.0798	0.0798	0.00	0.00	0.00
4	0.0802	C_2H_5OH*	5	0.0802	0.0800	0.00	0.25	0.24
5	0.0922	CH_3OH	3	0.0922	0.0922	0.00	0.00	0.00
6	0.1327	CH_3OH*	3	0.1327	0.1327	0.00	0.00	0.87

The solubility of sodium tetrafluoroborate. Method of analysis. First of all, we verified the possibility of determining $NaBF_4$ in solutions, by concentrating them in platinum crucibles, drying at 120-150° and weighing. In order to depress the hydrolysis of BF'_4 to part of the solution at the end of the evaporation we added 1-2 drops of a 35% solution of tetrafluoroboric acid. These experiments are designated by asterisks in Table 1.

The weighed portion of salts was evaporated twice with water, so that the possible influence of hydrolysis would show up more clearly. After weighing, the content of $NaBF_3OH$ in the precipitate was determined by titration

with alkali, after the addition of $CaCl_2$ and methyl orange. The results of the experiments are presented in Table 1.

The error incurred in the evaporation of the aqueous solutions containing added drops of HBF_4 did not exceed the possible error of the weighings. The hydrolysis of BF'_4 was depressed to a considerable degree. Moreover, the change of weight of the precipitate as a result of the reaction

$$NaBF_4 + H_2O \rightleftharpoons NaBF_3OH + HF\uparrow$$

seemed to be very negligible in the neighborhood of the molecular weights of $NaBF_4$ and $NaBF_3OH$. Further hydrolysis of the latter to boric acid, which was volatile with the water vapor, was prevented.

Solvolysis of $NaBF_4$ by the action of ethanol and methanol did not occur, and the addition of HBF_4 during evaporation seemed unnecessary. In the precipitates of experiments 4 and 6, where HBF_4 was introduced, obviously, traces of $BF_3 \cdot H_2O$ were observed.

Solubility of $NaBF_4$ in Water

By study of the solubility of the substance containing the slowly hydrolyzing complex ion, the following different values could be obtained:

a) the equilibrium solubility might be established so fast that the complex ion did not have time to hydrolyze to an appreciable degree; this value corresponded to the true solubility of the salt;

b) not only the equilibrium solubility, but also the equilibrium hydrolysis of the complex ion, was established; the value found for the solubility was higher than that in the first case, but also appeared to be an equilibrium value;

c) by establishment of the equilibrium solubility, we did not succeed in establishing the equilibrium hydrolysis of the complex ion; thus we obtained "solubility" values, depending on the duration of the experiment, and including among these values, those determined in variations (a) and (b).

TABLE 2

Solubility of $NaBF_4$ in Water

Sample No.	Temperature (in °C)	Length of time of saturation (in mins.) from beginning of solution of the salt	Length of time of saturation (in mins.) at a given temperature	Solubility (in %)
		Mixture 1: 5 g $NaBF_4$ + 5 ml of water		
1	0	125	85	41.96
2	0	295	250	41.77
3	0	485	445	41.96
4	0	605	565	42.09
			Average	41.95
		Mixture 2: 4 g $NaBF_4$ + 3 ml of water		
5	13.3	90	60	46.99
6	23.1	195	80	50.17
		Mixture 3: 6 g $NaBF_4$ + 4 ml of water		
7	25.0	130	105	50.73
8	50.0	180	35	57.42
9	35.0	305	70	53.76
10	20.0	415	60	49.28
11	11.0	525	60	46.00

For $NaBF_4$, the difference in the magnitude of the solubilities found for (a) and for (b) was not great, since the salt was very well dissolved, and the equilibrium hydrolysis constant of BF'_4 permitted us to determine the real solubility of the salt, i.e., that corresponding to case (a).

A test tube containing a mixture of water and an excess of $NaBF_4$ was agitated at room temperature for a period of 30-40 minutes, after which it was transferred to a thermostat, in which the contents of the test tube were mixed with a motor-driven stirrer.

For the experiments at 0°, a Dewar vessel filled with ice served as the thermostat, and for the other temperatures — the usual thermostat, with automatic regulation of the temperature to an accuracy of $\pm$ 0.05°, was employed.

The samples for analysis (0.5-1 g) were removed from the clear, supernatant solution with a pipet fitted with a cotton filtering plug, and transferred to a platinum crucible for weighing. After the samples were weighed, they were evaporated (toward the end of evaporation, 1 drop of 35% solution of HBF_4 was added), and dried to constant weight at 120-150°.

A series of determinations was carried out in one day for the same mixtures of $NaBF_4$ and water. The results of the determinations are provided in Table 2.

The experiments for mixture 1 confirmed that, even at 0°, the state of saturation is reached after 85 minutes. At higher temperatures and larger ratios of the quantities of salts to water, saturation should be attained still more rapidly. Demonstration of this was seen by the fact that all the values that we found were approached both from the side of saturation and from the side of supersaturation, and were concealed in the general fusion curve (Fig. 3). This demonstrates that for short periods of heating at 50°, the $NaBF_4$ did not hydrolyze to any considerable degree.

The solubility at 24° found by Caillat was quite exaggerated. The initial temperatures of crystallization were established with complete clarity for slightly supercooled solutions (0.03-0.2°), correcting both for the energy of stirring and for the introduction of ice:

% $NaBF_4$ in solution	10.94	20.02	29.87,
t° crystallization of ice.	−2.79	−5.50	−8.29.

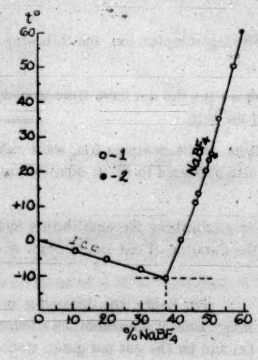

Fig. 3. Equilibrium diagram of the system $NaBF_4-H_2O$. 1) Authors' data; 2) Caillat's data.

The eutectic disturbance could be observed only in 29.87% solution, but in more dilute solutions, at the beginning of solidification of the eutectic, the quantities of ice separated were too large. The eutectic disturbance appeared still better (−10.69°) on cooling a 40.08% solution; on a cooling curve for this solution, we observed the temperature of the onset of crystallization of $NaBF_4$, which apparently was not averted, considering the small heat effects of this process. Analyzing samples of the solution, taken at the time of crystallization of the eutectic, it was found that the eutectic solution contained 37.12% $NaBF_4$.

The character of the equilibrium diagram of $NaBF_4-H_2O$ (Fig. 3) indicates that, also at low temperatures, no crystal hydrate of $NaBF_4$ forms. Thus, for sodium salts, the crystallochemical properties of the tetrafluoroborates and perchlorates, frequently described in the literature, are disturbing: it is known that sodium perchlorate forms a monohydrate which is stable at room temperature. By frequent freezing of 40% solutions of $NaBF_4$, neither by reason nor by observation could we detect a hydrate, not even a metastable hydrate.

Solubility of $NaBF_4$ in Anhydrous Ethanol

The solubility of $NaBF_4$ in anhydrous ethanol was considerably lower than in water or methanol.* The data are given in Table 3 and in Fig. 4. After the experiments, the mother liquor contained only traces of BF_3OH^-.

Solubility of $NaBF_4$ in Water-Ethanol Mixtures

Determinations were carried out at 0°, as described earlier, and at 50° —in the thermostat in which the hermetically sealed tube containing a mixture of $NaBF_4$ and the solvent was shaken "over the head." Results — Table 4, Fig. 5.

The content of $NaBF_3OH$ in the mother liquors was indeterminably small in all the experiments at 0°. At 50° it did not exceed 0.1-0.2%, increasing with an increase in the water content.

On the basis of Fig. 5, the yields of $NaBF_4$ on cooling the saturated water-ethanol solutions from 50 to 0°, were calculated. The results of the calculations given in Fig. 6 show that the yield of $NaBF_4$ (in % of the dissolved salts) increased substantially with an increase of the ethanol content up to 40-50 weight %. Since the yield of salts per 100 g of solvent of the water-ethanol mixtures still remained sufficiently high, then for the recrystallization of $NaBF_4$ the use of water-alcohol solutions, containing 40-50 weight % ethanol can be recommended.

In order to obtain c.p. $NaBF_4$, the following method, differing somewhat from that described earlier [1], can be recommended.

With intense cooling, hydrofluoric acid was introduced into the boric acid in a quantity smaller than that required for complete conversion of HF to HBF_4 (0.96-0.97 mole for 4 moles of HF). Into a cooled lead or paraffin beaker ~ 96% of the quantity of calcined salt, calculated for complete neutralization of the acid, was introduced with intense stirring, and ~90-92% of tetrafluoroboric acid was added gradually. After liberation of the larger part

* According to out determinations, the solubility of $NaBF_4$ in methyl alcohol of specific gravity d_4^{18} 0.8123, was equal to 2.86% at 0°, 4.17% at 25° and 5.15% at 40°. The water content in the methyl alcohol sample used could not sharply increase the solubility of $NaBF_4$.

TABLE 3

Solubility of $NaBF_4$ in Anhydrous Ethanol

Sample No.	Temperature (in °C)	Length of time of saturating (in min.)		Solubility (in %)	
		from beginning of saturation	at the given temperature	individual determination	average
		Mixture 1. 1 g $NaBF_4$ + 30 ml C_2H_5OH			
1	0.0	200	170	0.25	
2	0.0	415	385	0.33	
3	0.0	1770	1740	0.24	
4	0.0	3030	3000	0.29	0.28
		Mixture 2. 1.5 g $NaBF_4$ + 40 ml C_2H_5OH			
5	25.0	100	60	0.45	0.47
6	40.0	210	60	0.65	
7	40.0	210	60	0.63	0.64
8	60.0	375	60	1.02	
9	60.0	375	60	0.98	1.00
10	25.0	510	60	0.49	0.47
		Mixture 3. 1 g $NaBF_4$ + 10 ml C_2H_5OH			
11	50.0	275	230	0.82	0.82

TABLE 4

Solubility of $NaBF_4$ in Water-Ethanol Mixtures

Sample No.	Temperature (in °C)	Content of alcohol in the solution (in %)		Length of time of saturating (in min.)	Solubility of $NaBF_4$ (in %)	
		weight	mole		individual determinations	average
1	0.0	20.0	8.83	90	22.2	22.2
2	0.0	40.0	20.69	60	11.23	
3	0.0	40.0	20.69	90	11.30	11.27
4	0.0	60.0	36.92	120	6.04	
5	0.0	60.0	36.92	120	6.05	6.05
6	0.0	80.0	61.02	100	1.77	
7	0.0	80.0	61.02	100	1.85	1.81
8	50.0	20.0	8.83	50	46.66	
9	50.0	20.0	8.83	120	46.46	46.56
10	50.0	40.0	20.69	65	34.30	
11	50.0	40.0	20.69	135	34.00	34.15
12	50.0	60.0	36.92	135	20.11	
13	50.0	60.0	36.92	135	20.12	20.12
14	50.0	80.0	61.02	120	6.88	6.88

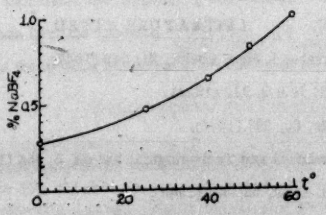

Fig. 4. Solubility of $NaBF_4$ in ethanol.

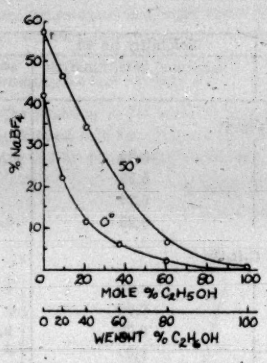

Fig. 5. Solubility of $NaBF_4$ in water-ethanol mixtures at 0 and 50° C.

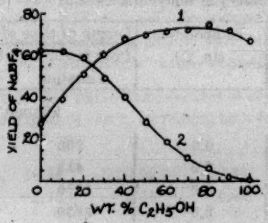

Fig. 6. Calculation of yield of $NaBF_4$ after recrystallization from water-ethanol solutions between 0 and 50°. A) Yield of $NaBF_4$; B) Wt. % C_2H_5OH. 1) Yield (%); 2) yield (grams/100 g of solvent).

of the carbon dioxide, the rest of the HBF_4 was added rapidly, and immediately after cessation of the liberation of carbon dioxide, a solution of concentrated alkali was added until a rose color was obtained with phenolphthalein. Such a method of concentration enabled us to obtain a concentrated solution, avoiding the considerable heating that is inevitable in neutralizations using concentrated alkali.

The solution was filtered off from the small residue of sodium fluoride and rapidly evaporated in vacuo or by passing a rapid current of heated air under the surface of the solution. Thus, it resulted that the solution remained weakly alkaline, lest we promote the acceleration of the hydrolysis of BF'_4 by the catalytic action of the acid.

The precipitate of $NaBF_4$ separating was recrystallized from a water-ethanol mixture, containing 40-50 weight % of ethanol, between 50-60° and 0- −10°. For obtaining the solvent, it was expedient not to evaporate the solution of $NaBF_4$ completely, but to add half the weight of alcohol to the solution of $NaBF_4$ saturated at 20-25°.

For synthesis of small quantities of $NaBF_4$, when it is not necessary to use the borate mother liquor, we could concentrate the initial solution to saturation at room temperature, add half the weight of alcohol, heat to 50-55°, filter and cool to 0° or somewhat below; thus, in the precipitate, about 80% of the sodium tetrafluoroborate contained in the original solution separated.

SUMMARY

1. In a solution containing 50 weight % of ethanol, the rate of decomposition of BF'_4 was less by a factor of 10.4 than in aqueous solution. The temperature coefficient of the reaction rate was practically unchanged.

2. In the system, $NaBF_4$—H_2O, the eutectic contained 37.12% $NaBF_4$ and solidified at −10.69°. There were no indications of the formation of a crystal hydrate of $NaBF_4$.

3. We determined the solubility polytherms of $NaBF_4$ in water, ethanol and methanol, and the solubility isotherm of $NaBF_4$ in water-ethanol mixture at 0 and 50°.

4. A method for obtaining pure $NaBF_4$ and the conditions of its recrystallization, were described.

LITERATURE CITED

[1] I. G. Ryss and M. M. Slutskaya, J. Phys. Chem., 21, 549 (1947).

[2] J. Berzelius, Pogg. Ann., 1; 169; 2, 113 (1824).

[3] R. Caillat, Ann. de Chimie, 20, 367 (1945).

[4] Handbook of Physical, Chemical and Technological Values, 5, 454 (1931).

[5] I. G. Ryss, Proc. Acad. Sci. USSR, 52, 421 (1946).

Received June 7, 1954

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INVESTIGATION OF THE REACTION OF ALUMINUM CHLORIDE AND PYRIDINE HYDROCHLORIDE IN AQUEOUS SOLUTION

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The compound having the composition $AlCl_3 \cdot C_5H_5N$, formed from aluminum chloride and pyridine, was obtained by Eley and Watts [1] by direct reaction of the components, in the form of a colorless, crystalline substance, easily decomposed by water. Pyridine, as is well-known, precipitates aluminum hydroxide from aqueous solutions of aluminum salts.

In hydrochloric acid solution, some weak bases form molecular compounds with aluminum chloride. For example, aluminum chloride forms a compound of composition $3N_2H_4HCl \cdot AlCl_3 \cdot 6H_2O$ [2], with hydrazine hydrochloride, considered to be the salt of chloroaluminic acid, $(N_2H_5)_3[AlCl_6]$. This compound was obtained by crystallization of a concentrated aqueous solution of aluminum chloride and hydrazine hydrochloride.

In order to determine the feasibility of forming analogous compounds of aluminum chloride with pyridine hydrochloride, we carried out an investigation of hydrochloric acid solutions of aluminum chloride and pyridine by physico-chemical methods of analysis.

EXPERIMENTAL*

The hexahydrate of aluminum chloride was used for the work. The chlorine content of the preparation was determined.

Found %: Cl 43.80. $AlCl_3 \cdot 6H_2O$. Calculated %: Cl 44.06.

The pyridine was dried over potassium hydroxide and distilled. The fraction having a b.p. of 114-115° was collected. Solutions of pyridine hydrochloride were prepared by mixing the calculated quantities of pyridine and hydrochloric acid.

We measured the specific gravity, viscosity and electrical conductivity of aqueous solutions of aluminum chloride containing pyridine hydrochloride, at 18 and 25°.

The solutions for the investigation were prepared by the method of isomolar concentrations, first suggested by Ostromislinsky [3]. The original, monomolar solutions of aluminum chloride and pyridine hydrochloride were mixed in different proportions, but to a constant sum of their volumes. Thus, in all the solutions studied, the sums of their molar concentrations were equal to one mole per liter.

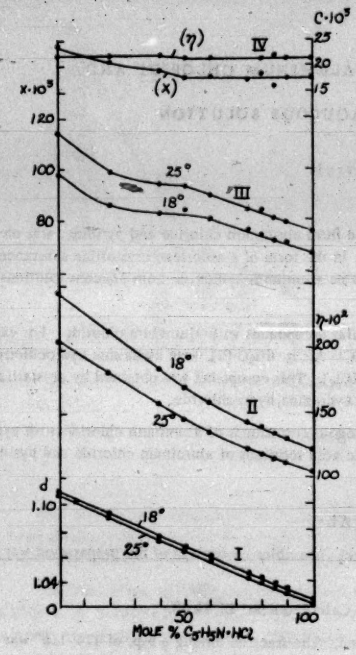
The specific gravity was determined with a pyknometer having a graduated, narrow neck and a capacity of 15 ml. The viscosity was determined, using an Ostwald viscosimeter. The specific electrical conductivity was measured in the usual way, using a lamp generator with optical indicator. The fluctuation of the temperatures of the water thermostat was $\pm$ 0.1°. Results of the measurements are presented in the Table and, graphically, in the Figure.

From the data obtained, we calculated the temperature coefficients of the viscosity and specific electrical conductivity. Calculation was made from the formulas $\frac{\eta_{18} - \eta_{25}}{\eta_{18}(25-18)}$ and $\frac{\kappa_{25} - \kappa_{18}}{\kappa_{18}(25-18)}$, where η_{18}, η_{25} and κ_{18}, κ_{25} are, respectively, the viscosity and the specific electrical conductivity at 18 and 25°.

DISCUSSION OF RESULTS

As seen from the figure, the specific gravity was found to have a linear relationship to the composition of the system. The viscosity decreased irregularly as the concentration of pyridine hydrochloride increased. At pyridine hydrochloride concentrations above 50%, the decrease of viscosity slowed down. The viscosity isotherms were somewhat concave toward the composition axis, and had a hardly-appreciable bend at the point corresponding to 50 mole-% of the components.

* The experimental work was carried out with the assistance of E. V. Ivchenko.



System $AlCl_3-C_5H_5NHCl-H_2O$. I) Specific gravity; II) viscosity; III) specific electrical conductivity; IV) temperature coefficients of viscosity (η) and electrical conductivity (κ).

The isotherms of the specific electrical conductivity had an S-shaped character, with a discontinuity at the same point. The temperature coefficient of the viscosity remained practically constant. The temperature coefficient of the specific electrical conductivity decreased as the pyridine hydrochloride concentration increased, the curve forming a minimum at a 50 mole % concentration of pyridine hydrochloride. At large concentrations, the temperature coefficient remained practically constant.

The data obtained indicated the formation in the system of a low-stability compound of aluminum chloride and pyridine hydrochloride, having a molar ratio of 1:1, i.e., the composition, $AlCl_3 \cdot C_5H_5NHCl$.

This compound should be considered as the pyridine salt of chloroaluminic acid, $C_5H_5NH[AlCl_4]$.

SUMMARY

1. The specific gravity, viscosity and electrical conductivity of aqueous solutions of aluminum chloride, containing pyridine hydrochloride, were measured at 18 and 25°.

2. The specific gravities of the solutions in this system were found to have a linear relationship to the concentrations of the solutions. With an increase of the mole fraction of pyridine hydrochloride, the specific gravity decreased. The viscosity isotherms were somewaht concave toward the composition axis, and had slight bends at a 1:1 molar ratio of the components.

3. The isotherms of the specific electrical conductivity were S-shaped, and had a discontinuity at the point corresponding to a 1:1 molar ratio of the components. This composition corresponds to the minimum appearing on the curve of the temperature coefficient of the electrical conductivity.

4. In the system, the low-stability compound, $AlCl_3 \cdot C_5H_5NHCl$, forms, and it is considered by the authors to be the pyridine salt of chloroaluminic acid, $C_5H_5NH[AlCl_4]$.

Specific Gravity, Viscosity and Electrical Conductivity of the System $AlCl_3-C_5H_5NHCl-H_2O$

Sample No.	$C_5H_5N \cdot HCl$ (in mole %)	Specific gravity d_4^t		Viscosity $\eta \cdot 10^2$ centipoises		Temperature coefficient of viscosity, $C_\eta \cdot 10^3$	Specific electrical conductivity, $\kappa \cdot 10^3 cm^{-1} \cdot em^{-1}$		Temperature coefficient of electrical conductivity, $C_\kappa \cdot 10^3$
		18°	25°	18°	25°		18°	25°	
1	0	1.1095	1.1076	244.6	206.6	22.2	97.6	113.8	23.7
2	20	1.0929	1.0905	213.4	180.4	22.1	86.3	98.9	20.9
3	40	1.0747	1.0730	185.3	156.7	22.0	83.1	94.5	19.6
4	50	1.0667	1.0651	170.4	144.6	21.6	83.8	94.2	17.7
5	60	1.0582	1.0560	159.5	135.5	21.5	80.3	90.4	18.0
6	75	1.0447	1.0430	143.7	121.6	21.8	75.7	85.1	17.7
7	80	1.0417	1.0393	139.9	118.9	21.5	74.1	83.8	18.7
8	85	1.0371	1.0348	134.2	113.8	21.7	72.2	80.4	16.2
9	90	1.0329	1.0306	130.4	110.8	21.5	70.6	79.2	17.4
10	100	1.0236	1.0220	121.7	103.3	21.6	67.5	75.8	18.0

LITERATURE CITED

[1] D. Eley and H. Watts, J. Chem. Soc., 1952, 1914.

[2] W. Pugh and M. Hotz, J. Chem. Soc., 1953, 2493.

[3] I. Ostromislensky, Ber., 44, 268 (1911).

Received May 17, 1954

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PHYSICO-CHEMICAL ANALYSIS OF SYSTEMS FORMED BY ALCOHOLS WITH ORGANIC ACIDS

I. DENSITY, VISCOSITY AND ELECTRICAL CONDUCTIVITY OF THE SYSTEM ACETIC ACID–ETHYL ALCOHOL

Z. S. Drutman

In physico-chemical diagrams, particularly in viscosity diagrams, a definite form reflects the different processes proceeding in the liquid system. Even such small interactions, as intermolecular and dipolar interactions, show up as some positive deviation from the normal viscosity isotherm [1]. Interactions in which chemical forces participate, where very often the chemical forces to some degree or other accompany intermolecular forces, obscuring them, are reflected most clearly by the viscosity isotherms.

Many intermolecular compounds are known, the origins of which are impossible to attribute to the action of one force or another. They appear to be the result of the operation of both intermolecular and chemical forces. Such physico-chemical interactions may be diverse, beginning with extremely weak forces, in which the reaction products have a definite influence on the properties of the system and may not be separated and identified, and ending with so much force that stable crystallizine compounds form.

Comparison of the results of investigations of very different systems shows that the physico-chemical diagram may not give any definite indication of the nature of the interactions in the system, even in the case of the small participation of chemical forces in this interaction.

Systems formed by organic acids and alcohols may serve as illuminating examples in this respect.

As shown by a whole series of investigations, the chemical process of esterification in such systems is preceded by another process, the physico-chemical process of solvation. These two processes proceed simultaneously in the system, but at different rates. Whereas the solvation process proceeds practically instantaneously, the esterification process proceeds, under normal conditions, in time. On the strength of this, it is possible to neglect the second process at least for some ten hours from the moment of formation of the system.

Such a peculiarity in the behavior of the system formed by organic acids and alcohols permits one to study these processes independently.

We studied the system of acetic acid–ethyl alcohol at two stages: in the first period of the formation, when it was possible to disregard the chemical interaction, and after the attainment of chemical equilibrium.

EXPERIMENTAL

The pure substances were prepared by generally acdepted methods, after which they were characterized by constants agreeing well with those given in the literature. The purified substances were stored in flasks with ground-glass stoppers and covers. The prepared solutions were weighed. Measurements were made at 0, 20, 40 and 60° with an accuracy up to 0.1–0.2°. The viscosity was measured with a viscosimeter of the closed type with times of discharge for water ranging from 180 to 600 sec at 20°. For measuring the specific electrical conductivity we used an optical indicator (a 6E5 lamp with amplifier). The measurements were carried out in vessels having good ground-glass stoppers and covers.

System Acetic Acid – Ethyl Alcohol During the First Period of Formation

The system has been studied at this stage by different authors and under various conditions. Some [2-4] studied the system in the pure state. Others [5, 6] studied it in the presence of an inert solvent, and found that in it the acid molecules were solvated by the alcohol molecules. The solvates forming in the system were shown to differ in composition only by the investigations of Izmailov and Spivak [6], who observed the presence in the system of a compound of 1:1 proportion, and the possible formation of still another compound with two molecules of alcohol, the 1:2 compound.

We studied the density, viscosity and specific electrical conductivity of this system.

TABLE 1

Density of the System Acetic Acid–Ethyl Alcohol During the First Stage of Formation

C_2H_5OH (in mole %)	d			
	0°	20°	40°	60°
0.00	–	1.052	1.028	1.008
6.78	–	1.036	1.017	0.9957
10.04	–	1.032	1.008	0.9872
12.95	1.042	1.021	1.002	0.9813
15.58	1.036	1.017	0.9965	0.9750
17.00	1.033	1.013	0.9942	0.9720
18.93	1.028	1.008	0.9862	0.9660
28.24	1.005	0.9900	0.9665	0.9425
31.80	0.9940	0.9760	0.9548	0.9342
35.50	0.9852	0.9663	0.9453	0.9250
38.72	0.9773	0.9562	0.9392	0.9163
43.06	0.9665	0.9510	0.9270	0.8990
49.41	0.9454	0.9227	0.9083	0.8906
54.13	0.9340	0.9176	0.9004	0.8750
60.75	0.9143	0.9000	0.8782	0.8603
69.69	0.8912	0.8742	0.8550	0.8360
79.88	0.8637	0.8475	0.8280	0.8104
89.96	0.8372	0.8183	0.8045	0.7876
100.00	0.8080	0.7930	0.7750	0.7592

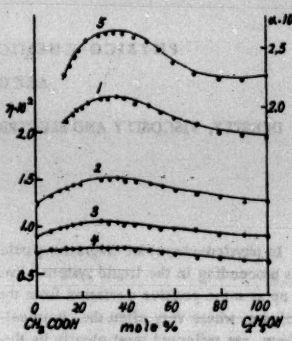

Fig. 1. Viscosity isotherms of the system $CH_3COOH-C_2H_5OH$ during the first period of its development at: 1) 0°; 2) 20°; 3) 40°; 4) 60°; 5) absolute temperature coefficient of the viscosity.

The results of the density measurements are given in Table 1. The density isotherms are represented by almost additively straight lines, with small curvatures at the composition axis in the acetic acid region.

The results of the viscosity and specific electrical conductivity measurements are illustrated in Figs. 1 and 2.

The viscosity isotherms at all temperatures are represented by S-shaped curves with maxima in the acetic acid region and with points of discontinuity at about 50 mole % ethyl alcohol. The maxima even at low temperatures had an extremely diffuse character and came at approximately 33 mole % of alcohol. At increasing temperatures, the maxima became more and more flat, being displaced toward the side of the more viscous acetic acid. The discontinuities on all the isotherms maintained their positions.

The curves of the absolute temperature coefficient of the viscosity (Fig. 1, Curve 5) repeated exactly the course of the viscosity curves.

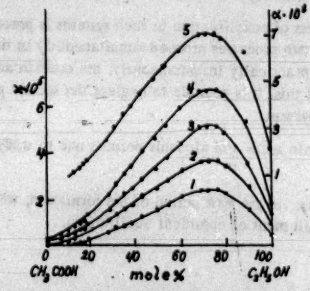

Fig. 2. Specific electrical conductivity isotherms of the system $CH_3COOH-C_2H_5OH$ during the first period of its development at: 1) 0°; 2) 20°; 3) 40°; 4) 60°; 5) absolute temperature coefficient of the electrical conductivity.

The specific electrical conductivity isotherms at all temperatures were slightly concave toward the composition axis in the region of acetic acid, and were considerably convex toward the composition axis in the ethyl alcohol region. The maxima on the isotherms did not change their positions as the temperature changed, and came at approximately 73 mole % of ethyl alcohol.

The curves of the absolute temperature coefficient of the electrical conductivity (Fig. 2, Curve 5) repeated the course of the curves of this property.

System Acetic Acid–Ethyl Alcohol on Attainment of Chemical Equilibrium

In order to bring the system to chemical equilibrium, we used the data of Trofimenko [7]. The prepared mixture was heated in sealed ampoules at 200° for 50-55 hours, after which the contents of the ampoules were examined for density and viscosity.

The results of the density measurements are given in Table 2. The relation of viscosity to composition is presented graphically in Fig. 3.

TABLE 2

Density of the System Acetic Acid–Ethyl Alcohol on Attainment of Chemical Equilibrium

C_2H_5OH (in mole %)	d			
	0°	20°	40°	60°
0.00	–	1.050	1.032	1.010
6.78	1.057	1.037	1.015	0.9960
10.04	1.050	1.030	1.010	0.9892
12.95	1.046	1.024	1.000	0.9820
15.58	1.038	1.018	0.9970	0.9758
17.00	1.035	1.020	0.9982	0.9725
18.93	1.032	1.012	0.9870	0.9660
28.24	1.002	0.9910	0.9692	0.9450
31.80	0.9948	0.9772	0.9556	0.9357
35.50	0.9847	0.9676	0.9462	0.9252
38.72	0.9770	0.9564	0.9384	0.9170
43.06	0.9660	0.9502	0.9279	0.9007
49.41	0.9472	0.9328	0.9098	0.8900
54.13	0.9352	0.9200	0.9000	0.8758
60.75	0.9158	0.9032	0.8800	0.8622
69.69	0.8915	0.8756	0.8552	0.8358
79.88	0.8635	0.8482	0.8283	0.8100
89.96	0.8368	0.8200	0.8030	0.7880
100.00	0.8082	0.7932	0.7764	0.7586

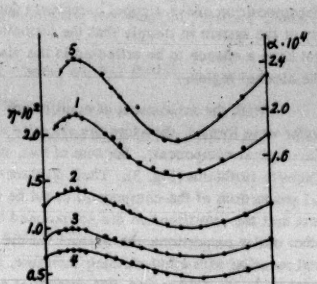

Fig. 3. Viscosity isotherms of the system $CH_3COOH-C_2H_5OH$ on attainment of equilibrium at: 1) 0°; 2) 20°; 3) 40°; 4) 60°; 5) absolute temperature coefficient of the viscosity.

The viscosity isotherms had an unusual form, showing diffuse minima in the alcohol region and diffuse maxima in the acid region. Neither the maxima nor the minima came at a rational proportion of the components. As the temperature increased, the maxima and minima again became more flat and somewhat displaced: the former toward the acid side, and the latter toward the alcohol side.

The curves of the absolute temperature coefficient of the viscosity (Fig. 3, Curve 5) duplicated the course of the viscosity curves.

DISCUSSION OF RESULTS

The results of studying the present system during the first stage of development, when the chemical interaction between acetic acid and ethyl alcohol could be neglected, indicated the presence in the system of interactions as a result of which solvates form. However, the statements of Udovenko [5] and Izmailov [6] that in the system only solvates having one molecule of acid to one or more molecules of alcohol are present, arouse doubts. On the other hand, if the presence of non-displaced discontinuities on the viscosity isotherms (Fig. 1) also indicates the formation in the system of rather stable solvates with 1:1 proportions of the components, then the maxima in the acid region on the viscosity isotherms and the curves of the temperature coefficient of viscosity indicate the formation of compounds with a predominating acid content. It is possible to account for the diffuseness of these maxima by both the considerable dissociation of the compounds in the system with methyl alcohol [8], and by the effect of the decomposition of associated molecules of the components. However, a more probable explanation seems to be the presence of some solvates containing two, three, and more molecules of acetic acid for each molecule of alcohol, and having extremely similar properties.

The presence in the system of solvates having predominating contents of alcohol is indicated by maxima in the alcohol region on the specific electrical conductivity isotherms (Fig. 2). Actually, the character of the curves does not differ at all in form from the curves obtained by Usanovich [9] for the system without the reaction of the components. But the presence of the same maxima in the curve of the temperature coefficient of the electrical conductivity indicates interaction of the components.

In order to satisfy ourselves of the presence of such an interaction, from the data on electrical conductivity, we calculated viscosity corrections for the conductivity. The data obtained are shown in Fig. 4. The maintenance of the maximum in the isotherms of the corrected electrical conductivities confirmed the existence in the system of solvates in which the alcohol content predominated.

The presence of such solvates was not reflected in the viscosity isotherms, possibly because the associated ethyl alcohol complexes decomposed in solution to a far greater degree than did the analogous acetic acid complexes. The process of decomposition of the alcohol complexes decreased the viscosity of the system so sharply that the formation of solvates did not have a chance to be reflected in the viscosity isotherms in the alcohol region.

With the attainment of equilibrium ethyl acetate and water were formed, therefore the viscosity was less than that of the original components. Because of this, minima formed on the viscosity isotherms (Fig. 3). Their displacement from rational 1:1 proportions of the components could be accounted for by the fact that the esterification did not proceed to completion. In other molar proportions, the acetic acid did not enter into chemical reaction with ethyl alcohol; therefore, the presence of the maxima in the acid region, not coming at a rational proportion of the components, could be considered as the result of the formation of solvated complexes from the components which were present in considerable quantities at equilibrium.

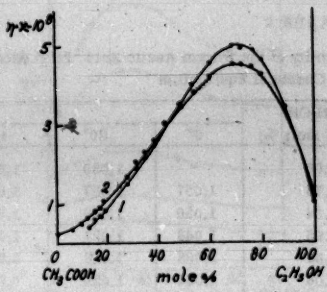

Fig. 4. Isotherms of the corrected electrical conductivity of the system $CH_3COOH-C_2H_5OH$ at: 1) 0°; 2) 60°.

At increased temperatures, the solvate complexes decomposed and the maxima flattened out. These complexes showed a considerably larger temperature coefficient of viscosity than did the products of the chemical reaction, which caused the maxima to become sharper when the temperature decreased, and caused the minima to be more sharply displaced toward the side of the rational 1:1 proportion of components, regardless of the fact that at this point the equilibrium was displaced toward the side of formation of the starting materials [10].

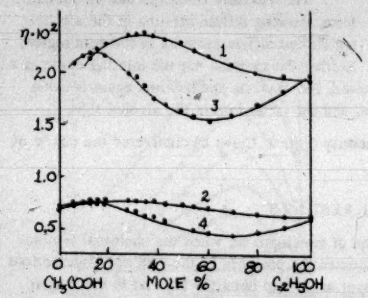

Fig. 5. Diagram comparing the viscosity isotherms of the system $CH_3COOH-C_2H_5OH$ at 0° and 60°. 1) and 2) During the first period of development; 3) and 4) on attainment of equilibrium.

The fact that on the same viscosity isotherms (Fig. 3), the same form reflected two entirely different processes, indicated that from the form of the physico-chemical diagram it is not possible to judge the nature of the processes proceeding in the system. In Fig. 5, there is a comparison of the results of the measurements of viscosity of the system, studied under different conditions at 0° and 60°.

From the figures, it follows that the viscosity isotherms provided no special features by which it was possible to judge the nature of the reactions occurring in the system.

SUMMARY

1. We studied the density, viscosity and specific electrical conductivity of the system acetic acid–ethyl alcohol at the first moment of its development, and the density and viscosity of the same system on attainment of equilibrium.

2. It was found that, during the first period of development of the system, solvates both with a predominating alcohol content and with a predominating acid content were formed. By this, the location and character of the maxima on the viscosity and specific electrical conductivity isotherms were specified, and also the nature of the relationship of their absolute temperature coefficients to the composition was indicated.

3. The chemical process of ester formation was reflected by the form of the minima in the viscosity isotherms, and by the curves relating the absolute temperature coefficient of the viscosity to the composition of the system, after attainment of chemical equilibrium.

4. By comparing the data obtained, it was possible to arrive at the conclusion that the form of the physico-chemical diagram does not give a basis for indication of the nature of the reactions occurring in the system.

LITERATURE CITED

[1] S. F. Babak, J. Gen. Chem., 20, 1568 (1950).*

[2] K. Hartwig, Wied. Ann., 33, 58 (1888).

[3] S. U. Pickering, J. Chem. Soc., 63, 998 (1893); Technical Encyclopedia, Handbook of Physical, Chemical and Technological Values, 6, 219 (1931).

[4] C. Bingham, C. F. White, A. Thomas, L. L. Cadwell. Z. phys. Chem., 83, 641 (1913).

[5] V. V. Udovenko and S. F. Babak, J. Gen. Chem., 18, 572 (1948).

[6] M. A. Izmailov and L. L. Spivak, Proc. of the Inst. of Chem. of Kharkhov State University, 7, 153 (1950).

[7] A. P. Trofimenko, J. Phys. Chem., Supplement, 1947, 271.

[8] A. S. Naumova, J. Gen. Chem., Supplement II, 792 (1953).

[9] M. I. Usanovich, Proc. Conference Phys. of Western Siberia, 5, 11 (1935).

[10] A. P. Trofimenko, J. Phys. Chem., Supplement 1947, 296.

Received May 31, 1954

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* See Consultants Bureau Translation, page 1629.

PHYSICO-CHEMICAL ANALYSIS OF THE SYSTEM ALLYL MUSTARD OIL–ETHYL ALCOHOL

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Earlier we investigated the system allyl mustard oil–piperidine [1], for the purpose of elucidating the nature of electrolytic dissociation in non-aqueous systems, and observed that, as a result of the reaction between the components, the CNS^- ion was formed; this was rather unexpected.

In order to find out whether allyl mustard oil forms thiocyanate ion during reaction with other substances also, we undertook the investigation of the system allyl mustard oil–ethyl alcohol.

We began our investigation with a physico-chemical analysis of the system $C_3H_5NCS-C_2H_5OH$, in order to define the character of the interaction between the components. For this purpose, the following properties of the above-mentioned system were studied: viscosity, density, surface tension, index of refraction and electrical conductivity.

EXPERIMENTAL

Chemically pure allyl mustard oil was subjected to distillation, with separation of the 149.5-150.3° fraction. The product obtained in this way was a light yellow liquid with d_4^{20} 1.0123 and n_D^{20} 1.5300.

Anhydrous alcohol was obtained by treating an alcohol distillate three times with a small quantity of metallic sodium, followed by distillation. The product obtained was distilled to eliminate traces of sodium ethylate (d_4^{25} 0.79010).

TABLE 1

Viscosity of the System Allyl Mustard Oil–Ethyl Alcohol

C_3H_5NCS (in mol %)	η	
	20°	−15°
0	0.0165	0.0293
10	0.01430	0.02765
20	0.01310	0.02695
27.8	0.01290	–
30	–	0.02464
33	0.01293	–
40	0.01208	0.02402
50	0.01040	–
67	0.00801	0.01673
80	0.00739	–
90	–	0.01297
100	0.00725	0.01242

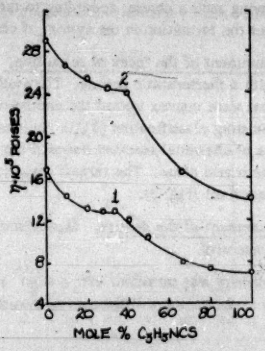

Fig. 1. Viscosity of the system allyl mustard oil–ethyl alcohol. 1) 20°; 2) −15°.

Measurement of viscosity. The viscosity was determined in an Ostwald viscosimeter of the closed type at 20 and −15° ± 0.1°. The results of the measurements are presented in Table 1 and in Fig. 1.

The viscosity isotherms obtained were made up of two branches, which were convex toward the abscissa and met at a composition of approximately 33 mole % of C_3H_5NCS.

Viscosity isotherms of such a shape, according to the standard classification [2, 3], indicate the presence of a chemical reaction between the components, and are characteristic of the irrational system, in which the number of molecules does not change as a result of reaction.

Measurement of surface tension. The surface tension was measured by the Kantor method, modified by Rebinder with the use of a "tandem", recommended by Trifonov [4] for finding the fractional vaporization, at the time of measurement, in the closed type vessel with a mercury seal that he described. The determinations were made at 20, 0 and −18.3°.

The results of the measurements are presented in Table 2 and Fig. 2.

TABLE 2

Surface Tension of the System Allyl Mustard Oil–Ethyl Alcohol

C_3H_5NCS (in mole %)	σ			
	Calculated from the Stakhorsk equation (20°)	20°	0°	−18.3°
0		22.6	25.2	29.08
10	23.42	24.03	26.09	28.04
20	24.3	25.25	27.06	28.72
27.8		26.05	–	–
30	25.25	–	27.58	30.56
33	–	27.25	–	–
40	26.28	27.71	29.18	31.02
50	27.4	28.58	29.82	31.36
67	29.53	29.86	31.25	32.63
80	31.41	32.11	32.51	35.09
90	33.02	33.27	–	–
100	–	34.81	36.82	42.94

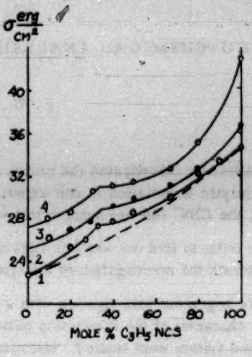

Fig. 2. Surface tension of the system allyl mustard oil–ethyl alcohol. 1) Calculated from the Stakhorsk equation; 2) 20°; 3) 0°; 4) −18.3°.

The surface tension isotherms obtained gave positive deviations from the Stakhorsk isotherms for normal systems (broken line), and were similar to the viscosity isotherms, which consisted of two branches convex toward the composition axis, and having a break which comes at a composition of 30-40 mole % C_3H_5NCS. A surface tension isotherm having such a course, according to the classification of Trifonov [5], is characteristic of irrational systems, i.e., indicates the formation in the system of chemical compounds that are partially dissociated into their components.

Measurement of the index of refraction. The index of refraction was measured with an Abbe refractometer equipped with a thermostatic device. The isotherms of n_D (Fig. 3), constructed from the data in Table 3, consisted of curves that were convex toward the composition axis. Such a shape of the index of refraction isotherms, according to the existing classification [2], in conjunction with the isotherms of other properties of the system, indicates the presence of chemical reaction between the components, with formation of compounds that are partially dissociated in the liquid phase. The largest deviation from additivity corresponded to a composition of 30-40 mole % of allyl mustard oil (Fig. 3).

Measurement of the density. Measurement of the density of the mixed system was made chiefly for calculation of the viscosity.

The density was measured with a Reno pykuometer; the data obtained are given in Table 4 and in Fig. 4. The density isotherm was a little convex toward the composition axis.

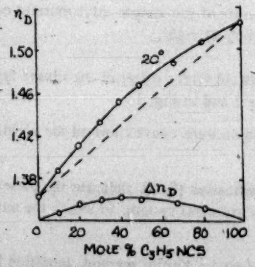

Fig. 3. Index of refraction of the system allyl mustard oil–ethyl alcohol.

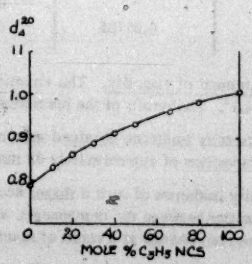

Fig. 4. Density isotherm of the system allyl mustard oil–ethyl alcohol.

Measurement of the electrical conductivity. The specific electrical conductivity was measured by the Kohlrausch method by an improved arrangement, usually used for measuring the conductivity of non-aqueous solutions. The vessel had non-platinized platinum electrodes.

The frequency generator also was completely shielded from the conducting system. For the slide wire, a rotating bridge with a conducting wire 3 m long was used. The results of the measurements are given in Table 5. The electrical conductivity isotherms were constructed on the basis of these data (Fig. 5), and consisted of curves having maxima that come at a composition of 33 mole % of C_3H_5NCS.

TABLE 3

C_3H_5NCS (in mole %)	n_D^{20}
0	1.3625
10	1.3876
20	1.4105
30	1.4325
40	1.4523
50	1.4677
67	1.4885
80	1.5085
90	—
100	1.5292

TABLE 4

C_3H_5NCS (in mole %)	d_4^{20}
0	0.7901
10	0.8300
20	0.8602
30	0.8879
40	0.9127
50	0.9342
67	0.9627
80	0.9869
100	1.0123

Trifonov considered a κ isotherm having such a shape, as characteristic of both an irrational system, and a normal system in which the components on mixing do not enter into chemical combination and do not alter their degrees of association, if they are associated [6].

It is well-known that reactions between organic substances proceed very slowly. Trifonov and Voskresenskaya found in their work that the electrical conductivity in non-aqueous systems depends strongly on the length of time the solutions have been stored [2]. The value of the time factor in establishing equilibria in systems, especially organic equilibria, was emphasized also in the works of Komilov [7] and Ravich [8].

We attempted to determine the conductivity of freshly prepared mixtures of our system, and also solutions that had been standing 1-2 weeks, but κ was found to be very small. Measurements of the electrical conductivity, made after the mixture had been standing for two months, gave values for κ of the order of $1 \cdot 10^{-4}$ Ω^{-1} cm^{-1}. However, as we showed by further measurements, these values do not by any means appear to be limiting values. After 5 months,

TABLE 5

C_3H_5NCS (in mole %)	$\kappa \cdot 10^5$ measured after the mixture had been standing for a period of		
	2 months	5 months	8 months
10	6.06	31.11	43.0
20	11.8	42.03	—
27.8	—	49.6	—
30	12.7	—	100
33	—	52.67	—
40	17.4	51.70	—
50	16.1	44.7	93
67	11.7	—	65
80	7.5	—	—
90	3.4	4.1	—

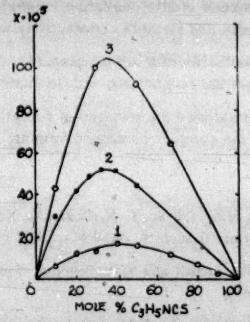

Fig. 5. Electrical conductivity of the system allyl mustard oil—ethyl alcohol at 20°, after standing for a period of: 1) 2 mos.; 2) 5 mos.; 3) 8 mos.

the maximum electrical conductivity was equal to $5.1 \cdot 10^{-4}$ Ω^{-1} cm^{-1}, and after 8 months it reached a value of $1 \cdot 10^{-3}$ Ω^{-1} cm^{-1}, i.e., was equal to the electrical conductivity of 0.01 N KCl. As is well-known, both components of the system seem to be practically non-conducting, the specific conductivity of both ethyl alcohol and allyl mustard oil being $< 10^{-9}$ Ω^{-1} cm^{-1}.

Further standing of the mixture did not produce an appreciable increase of the conductivity. Establishing the presence of a rather high electrical conductivity in the system, we naturally considered it necessary to find out whether or not C_3H_5NCS forms a conducting complex with alcohol, where the anion of the complex appears to be the CNS^- ion, and is analogous to that given by reaction with piperidine. A qualitative reaction for thiocyanate-ion in the freshly prepared solutions, and also in those that had been standing for several days, gave negative results. The solutions that had been standing for 2 months gave a weak reaction for CNS^-, and the same mixture that had been standing for 5 months and longer, gave a strong reaction, arousing no doubts as to the validity of the reaction of thiocyanate-ion and $FeCl_3$, $CuSO_4$, etc..

Thus, both the electrical conductivity of the mixture and the concentration of the CNS^- ions increase slowly with time.

In spite of the fact that the mixture was stored in a desiccator, in a bottle closed with a ground-glass stopper, a doubt might still arise as to whether moisture from the air might have got into it, because of the great hygroscopicity of the alcohol. If water did get in, it might lead to hydrolysis of the oil, and as a result, strongly distort the results.

In order to check this, we prepared several mixtures in ampoules, which were immediately sealed. After storing the sealed ampoules for five months, we measured the electrical conductivities of the mixtures, and they agreed very closely with the values obtained for solutions stored under the ordinary conditions.

DISCUSSION OF RESULTS

The isotherms of all the properties that were measured for the system studied indicated that the allylic mustard oil enters into chemical reaction with ethyl alcohol. The fact that, with a change of temperature, a break in the curve or a maximum on it is hardly displaced at all, indicates that the system approaches a rational system. Since the discontinuity in the viscosity and surface tension isotherms, the maximum on the electrical conductivity isotherms, and the largest deviation from additivity on the index of refraction isotherm, correspond to a composition of 33 mole % of allylic mustard oil, the composition $C_3H_5NCS \cdot 2C_2H_5OH$ can be ascribed to the compound forming.

The system had a rather high conductivity. The isotherms that we constructed for the molar electrical conductivity, presented an anomalous course, and consequently, neither the alcohol nor the oil appeared to be electrolytes. The current, obviously, was conducted by their compound-complex, the anion of which appears to be the thiocyanate-ion. We proved the presence of the CNS^- ion in the system, apart from the qualitative reaction, by making an experiment on electrolysis of the mixture in an apparatus having a platinum cathode and an iron anode; several minutes after the beginning of the experiment, a characteristic blood-red coloration appeared around the iron anode.

SUMMARY

1. The system of allyl mustard oil—ethyl alcohol was investigated. The viscosity, surface tension, index of refraction, density and electrical conductivity were studied.

2. The isotherms of all of the properties of the system that we studied indicated the presence of a chemical reaction between the components, with formation of a compound of the composition $C_3H_5NCS \cdot 2C_2H_5OH$.

3. We established the presence of a relatively high conductivity in the system, which was dependent on the dissociation of the complex compound forming, the anion of which, apparently, was the thiocyanate-ion.

LITERATURE CITED

[1] S. P. Miskidzhyan, F. N. Kozlenko, Reports on the Scientific Work of Members of the All-Union D. I. Mendeleev Chemical Society, Acad Sci. USSR Press, No. 1, 37 (1953).

[2] V. Ya. Anosov and S. A. Pogodin. Fundamental Principles of Physico-Chemical Analysis, Acad. Sci. USSR Press (1947).

[3] N. A. Trifonov, Bull. Sector Phys.-Chem. Anal., Acad. Sci. USSR, 14, 193 (1941).

[4] N. A. Trifonov and S. P. Miskidzhyan, J. Gen. Chem., 17, 1231 (1947).

[5] N. A. Trifonov, Sci. Rep. Kazan State Univ., 108, 3 (1948).

[6] N. A. Trifonov, Bull. of the Perm Biol. Sci.-Research Inst., 7, 45 (1931).

[7] N. Kornilov, Bull. Sector Phys-Chem. Anal, Acad. Sci. USSR, 20, 294 (1950).

[8] G. B. Ravich, Prog. Chem., 9, 1117 (1952).

Received February 15, 1954

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DUAL REACTIVITY AND TAUTOMERISM

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According to current ideas, the capacity of many organic substances for the formation of two (several) series of derivatives corresponding to the structures of two (several) isomeric forms of the substance – called its dual reactivity – seems to be a specific property of tautomeric substances. We subsequently show that such a definition of dual reactivity is limited in nature, although it includes the cases of tautomerism that are most important from the viewpoint of science, and thus we expand this definition; in the beginning we shall consider the mutual relationships of dual reactivities and equilibrium isomerism.

It is well known that the historical concept of tautomerism, or equilibrium isomerism, was evolved as a result of studying the dual reactivities of such substances as octylene in media of sulfuric acid, hydrocyanic acid, ethyl acetoacetate, isatin, quinoneoxime, etc.

Butlerov [1], studying the action of sulfuric acid on tertbutyl alcohol, found that the octylene obtained enters into chemical reaction in accordance with the two different structural formulas. A detailed study of the problem showed that this property is connected with the presence of two isomeric octylenes, and that between both the octylenes and the alcohols corresponding structurally to them, there is a reversible mutual transformation, which leads to the formation of an equilibrium mixture of the isomeric substances. Generalizing the observations made, Butlerov wrote: "In some cases it is possible also to find such substances, the mass of which includes appreciable numbers of isomeric molecules of different chemical structures – molecules which are constantly 'competing' between their mutual rearrangements from one structure to another – and, because of the molecule's tendency for rearrangement, its entire mass will, it is clear, undergo reactions characteristic of one structure or the other, depending on the nature of the reagent to whose influence it is subjected, depending, so to speak, on the direction in which this reaction takes place. Such molecules of dual structures* are, for example, cyanic acid, hydrocyanic acid, etc."

Thus, according to Butlerov, the phenomenon of equilibrium isomerism exists, and as a result of it, equilibrium mixtures of isomers appear to have the capacity to undergo reactions characteristic of the structures of each of the isomers, i.e., they have dual reactivities. This position is indisputable. It is possible, without much difficulty, to show many examples of how the presence of equilibrium isomerism produces dual reactivity. We recall the reactivities of ethyl acetoacetate and other ketoenols, aliphatic nitro compounds and many other classes of tautomeric substances. In accordance with the concept of Butlerov, tautomerism properly appears to be determined by equilibrium isomerism.

However, it is entirely proper to pose the question as to whether the concept advanced is effective in reverse, i.e., whether the dual reactivity always appears as a result of equilibrium isomerism, and, consequently, whether it is possible, by observing the dual reactivity, to reach a definite conclusion concerning the presence of equilibrium isomerism – tautomerism. Organic chemistry, at the end of the XIX and the beginning of the XX centuries, gave a positive answer to this question.

In his time, Laar [2] described a tautomeric phenomenon in which a substance reacts in accordance with, not one, but two possible structural formulas, i.e., the phenomenon of dual reactivity. It is well known that he did not consider the reason for this phenomenon to be equilibrium isomerism, but rather a special condition of oscillation of the atoms of the tautomeric substance. Later, thanks to the work of Claisen [3] and Wislicenus [4], the Laar theory was refuted and the concept of tautomerism as equilibrium isomerism triumphed. The capacity of a substance for dual reactions was adopted as a fundamental criterion of the presence of tautomeric behavior. The well-known formulation of K. Meyer [5] read: "Tautomeric substances form two series of derivatives, developed according to two isomeric formulas: these formulas differ from each other by the position of a hydrogen atom and – one or more double bonds."

The origin of such views becomes clear, if one considers that a large number of tautomeric (according to Knorr [6]), "allelotropic" mixtures of substances can be accounted for by dividing them into individual isomeric ("desmotropic") forms: acetyldibenzoylmethane, ethylformylphenylacetate, ethylmesityloxidoxalate, ethyldiacetylsuccinate, benzoylcamphor, phenylnitromethane, ethyl acetoacetate, acetylacetone and many others. For a

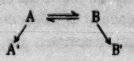
* Butlerov's expression "dual structure" must be understood, as is evident from the sense of the words employed and the entire spirit of Butlerov's theory of chemical structure, in the sense that each isomer has two separate structures, present in equilibrium mixture.

great number of keto-enols, although they have not been successfully isolated in the desmotropic form in the pure state, it has been possible to demonstrate their presence in solutions or melts by analytical or physico-chemical methods. All of these substances also have dual reactivities.

The conclusion arrived at includes the apparently valid assumption that, also in all other cases of dual reactions, the cause lies in the presence of mixtures of tautomeric forms in solutions or melts, each of which forms its series of derivatives. If the presence of these forms cannot be demonstrated by their isolation in the pure state or by some other method, then it is because there is too rapid a rate of mutual transformation, or because the position of the equilibrium is too strongly displaced toward the side of one of the forms (so-called "pseudomerism"), or finally, because the means used for the investigation are not sufficiently precise. Dual reactivity was assumed to be a necessary and sufficient condition for tautomerism, but even the concept of tautomerism began to imply not so much equilibrium isomerism, as dual reactivity.

In order to illustrate this assumption, we can cite the statement of the well-known expert of chemical literature, P. P. Shorygin. In the second edition of his book, "Progress of Organic Chemistry," published in 1932, he wrote: "The contemporary definition of tautomerism is this: this phenomenon consists of the fact that an organic compound gives 2 series of derivatives, corresponding to 2 fundamental structural formulas which differ from each other essentially by the position of one (or several) atoms of hydrogen, and by the presence or absence of one (or several) double bonds, it being impossible to separate the compound in the free state into its isomeric forms, the presence of the 2 forms being inferred only from their reactions" [7]. The idea of the complete correlation of tautomerism and dual reactivities was also assumed on the basis of accounts given in the well known book of J. W. Baker, "Tautomerism" [17].

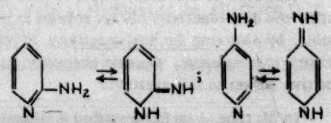
Finally, the last logical step in the equating of dual reactivities and tautomerism was acceptance, a priori, of the fact that, in all cases when two series of derivatives form, all of the derivatives having the structure of one of the possible tautomeric forms arise only from that form, and all the derivatives having the structure of the second possible tautomeric form, arise from the second form. Schematically, this may be represented as:



Scheme I

If we consult one of the better textbooks of organic chemistry – the book by Chichibabin, or the well-known book by Hückel, we will find the assertion that all keto derivatives of ethyl acetoacetate originate from its keto form, and all enol derivatives – from its enol form. This assumption has never been demonstrated, but it is considered to be self evident.

The textbook statements of these concepts induced organic chemists to carry out many valuable investigations, and many new types of tautomerism were discovered. By way of example, we can cite the discovery by Chichibabin, in the twenties, of the tautomerism of α- and γ-aminopyridine [8]:



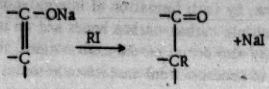
However, along with the successful results obtained by application of these concepts, in many cases there was conflict with the facts. Then, for the sake of maintaining the concepts, more or less plausible hypotheses of the reaction mechanisms were proposed, which invariably included the arbitrary assumptions. We can give several examples.

Concept of pseudomerism. This concept was introduced into science in its most clear form at the end of the last century by Knorr [9], and was used to account for the dual reactions of substances for which no method had succeeded in establishing the presence of tautomeric equilibria. The assumed explanation included the recognition of the existing limited displacement of tautomeric equilibria, when the concentration of one of the isomeric forms is "immeasurably" ("vanishingly") low, but this isomeric molecular form is distinguished by unusually high reactivity. The rapidity of establishment of equilibrium leads to the conclusion that the substance shows a dual reactivity. This point of view was developed most consistently in the twenties by Ingold and Thorpe [10]. Recently, it has been analyzed by Hückel [11]. It was his opinion that the position of the equilibrium A ⇌ B may be "anywhere" and that it will still be possible to treat the conversion of A into B' in terms of pseudomeric conversion: A ⇌ B → B', having only to assume sufficiently high rates of conversion.

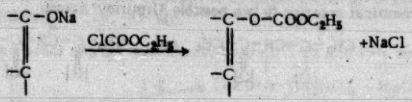
In the concept of pseudomerism, the criticism of which we present below, was included, the essentially

unscientific tendency to explain the mechanism of the reaction on the basis of assumptions of the existence of stages undemonstrable in principle, for on such a basis it was easy to construct an incorrect explanation, the weightiest argument for which was the impossibility of proof postulated in this explanation.

Another example. It is well known that alkali salts of the keto enols exist in the form of salts of the enol form. Not one example is known of structural isomerism of the salts of keto enols depending on a different position of the metal atom. Likewise, not one sodium or potassium derivative of the keto form of a keto enol is known. Moreover, in all alkylation reactions of alkali (and other) salts of the keto enols, the C-derivatives form, i.e., the derivatives of the ketonic forms of the substances:

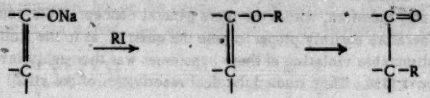


Only a few acylation reactions (for example, ethyl chlorocarbonate) lead to O-substitutions:



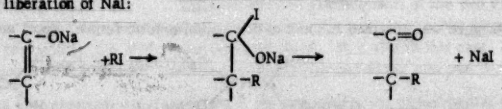
Consequently, a dual reactivity is present which is difficult to explain by assuming that the keto derivatives originate from the keto form, and the enol derivatives – from the enol form.

Various arbitrary assumptions as to the mechanism of reaction have been made from time to time to sustain this hypothesis. The hypothesis of Claisen [12] was based on the assumption of initial O-substitution, followed by rearrangement:



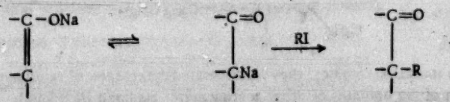
However, this hypothesis was refuted because of the inability of the simple esters of the enols to undergo such a rearrangement [13].

The hypothesis of Michael [14] included the assumption of an initial addition of alkyl halide to the multiple bond of the enolate, followed by liberation of NaI:



However, this hypothesis was refuted by the incapacity of the alkyl halides, under the conditions of the reaction, to alkylate the keto enols (ether or alcohol medium, presence of alcoholate, etc.) by adding to the multiple bond [15].

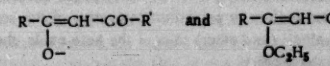
The hypothesis of Chelintsev [15a]-Hückel [15b] included the assumption of the pseudomerism of the alkali enolates:



However, this hypothesis also was not proved: it included the assumption of the existence of metallo-organic derivatives of the keto form, the sole proof of which was the phenomenon of C-alkylation, which explained it. Consequently, there is an erroneous chain of reasoning.

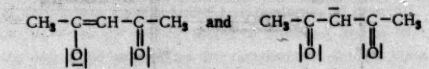
The concepts as to the ionic reactions of the salts of tautomeric substances developed by Arndt and Eistert [16] and accepted by Baker [17] represents to some degree a result of this situation. According to these concepts, the non-dissociated salt of the keto enol does not enter into reactions of alkylation or acylation, but its anion, the charge of which is distributed between the oxygen atom and the carbon atom (mesomeric ion), does. Consequently, in these

reactions, electrophilic reagents may attach not only to the oxygen atom, but also to the carbon atom, and, depending on the nature of the reagent and the reaction conditions, may form both C- and O- derivatives. However, these assumptions contradict the fact that the anions of the β-dicarbonyl compounds have definitely enolate structures. On the basis of spectral properties, they are characterized by their great resemblance to the corresponding O-alkyl derivatives of the enols:



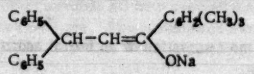
by their capacity for rapid addition of bromine, by their formation of internal-complex salts, and by other properties which characterize them as anions having multiple carbon-carbon bonds and an ionic charge on the oxygen atom. If some (small) increase of the electron density also occurs on the carbon atom, then it is necessary to assume that during the process of C-alkylation, a change of structure from enolate to ketonic, occurs.

Henecka [18] stated the point of view of Arndt differently. To the anion of the keto enol he attributed the capacity of entering into chemical reaction in two possible "limiting" forms:

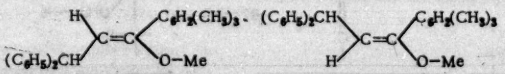


Depending on the nature of the reagent, and the conditions of the reaction medium, the anion reacts in one or the other of the limiting forms specified by its dual reactivity. Essentially, here the possibility of electronic tautomerism is to be considered – a hypothesis that has no experimental basis and conflicts with contemporary concepts of chemical structure.

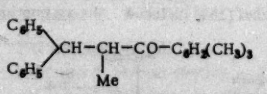
Thus, it is impossible to find an uncontradictory explanation of the numerous phenomena of dual reactivity within the limitations of the generally-accepted hypothesis that each tautomeric form gives rise to derivatives of corresponding structure, nor, therefore, within the more general concept of the complete identity of dual reactivity and tautomerism. It is therefore entirely proper to pose the question as to the limits of applicability of these hypotheses. The first indisputable violation of these hypotheses was thoroughly investigated by Nesmeyanov, Sazonova, Landor, and Vasilyeva [19]. They studied the dual reactivities of the alkali (lithium and sodium) and magnesium enolates of diphenylpropiomesitylene



This substance was obtained in each of two stereoisomeric forms: No. 1 and No. 2 (cis- and trans-):

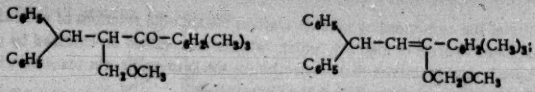


Under the specific conditions studied, the stereoisomers were incapable of reversible conversion, and consequently, the keto form was absent, because its presence with the enolate form at equilibrium would inevitably bring about their mutual transformation:



Thus, for these metallic enolates, they demonstrated the absence of tautomeric relationship as seen in the keto-enol tautomerism of the enolates of ethyl acetoacetate, assumed by Hückel:

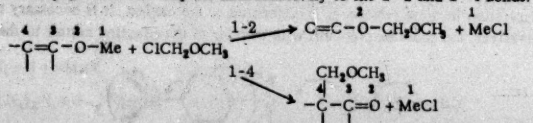
However, for each stereoisomeric series of enolates, they characterized the dual reactivity of the sodium derivatives of the keto-enols: they had the capacity of forming both C– and O–derivatives, on alkylation and acylation under suitable conditions, for example:



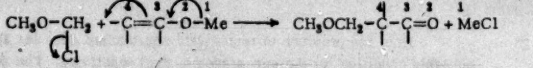
moreover, the O-derivatives formed in two stereoisomeric forms, corresponding in spatial configuration to the original enolates. Thus, for the benzoylated enolate No. 1, one benzoyl derivative formed, but from enolate No. 2 – the other stereoisomeric benzoyl derivative formed. Both stereoisomers were obtained without contamination by the other. Both benzoyl derivatives, on saponification, naturally formed the original diphenylpropiomesitylene. The keto derivative always was produced in one form, regardless of which stereoisomer of the enolate was obtained in the reaction.

The work of Nesmeyanov, Freidlina, Borisov et al., showed that the appearance of the dual reactivity (capacity of the enolates obtained for formation of C– and O–derivatives) is not necessarily due to the presence of equilibrium isomerism. The dual reactivity in the present case and in many other cases has another cause. According to Nesmeyanov [20] it appears as a result of the presence of conjugated systems of bonds (multiple or simple), in the molecule, in the case considered: $-\overset{4}{C}=\overset{3}{C}-\overset{2}{O}-\overset{1}{Me}$.

The presence of conjugated bonds imparts dual reactivity to the 1–2 and 1–4 bonds:



In the first case, the substitution reaction proceeds on that atom in the molecule from which the old substituent (metal atom) was removed. In the second case, the new substituent does not enter on that atom of the molecule from which the old substituent was removed, but on the carbon atom occurring at the other end of the conjugated system. The course of the reaction in the second case was characterized by Nesmeyanov as proceeding with transfer of reaction center:



The acyl- or alkyl-cation (new substituent) attacks the carbon (4) atom, to which, at the moment of reaction there is transferred the electron pair, liberated at the break of the O-metal bond and necessary for formation of the new bond. The conjugated system, thus, readily promotes the electromeric displacement of the two electron pairs of the 1-2 and 3-4 bonds. Even if we assume the presence of some fractional charge on the carbon atom of the system outside the reaction (it may be only negligible), the situation remains the same, as also in this case, at the moment of reaction, there must necessarily occur the envisaged transference (redistribution) of the electron density.

The principle value of the investigations cited includes, in the first place, the experimental evidence of the possibility of the formation of two series of derivatives without equilibrium isomerism. Both series of derivatives (keto and enol) arise here from the enol form. Secondly, the value of this work includes the fact that, according to the example of the metallic derivatives of typical keto-enol systems, precisely demonstrated cases were found where there was non-observance of the law: keto derivatives arise from the keto form, and enol derivatives from the enol form. In the examples considered, both the keto and enol derivatives formed from the enol form. A general scheme of a similar type of dual reaction may be written as (A-ketone, B-enol):

(Scheme 2a)

Other examples of the presence of dual reactivities with absence of tautomeric equilibria, seem to be the reactivities of the mercury-organic derivatives of aldehydes and ketones of the types $ClHgCH_2CHO$ and $ClHgCH_2COCH_3$, studied by Nesmeyanov, Lutsenko, Perevalov, Tumanova, Vereshchagin [21]. These substances, undoubtedly, have ketonic (aldehydic) structures. Thus, on reduction they form the corresponding mercurized alcohols, for example, $ClHgCH_2CH_2OH$. The mercury atom in them is bound by a non-ionic metallo-carbon bond. The absence of the tautomer in the sense of:

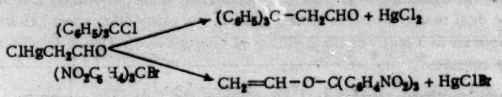
demonstrates the stability of the corresponding keto derivatives toward cold solutions of permanganate (consequently, the absence of the unsaturated enolate of mercury, which, without fail, should be oxidized by permanganate). Moreover, these substances have a dual reactivity that is specific for the keto-enols. On reaction with bromine, the mercury atom is replaced by bromine with formation of the C-derivative:

$$ClHgCH_2CHO + Br_2 \longrightarrow HgClBr + BrCH_2CHO,$$

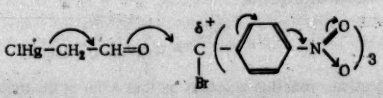
with a wide series of acyl halides these substances form O-derivatives (vinyl ethers):

$$ClHgCH_2CHO + RCOCl \longrightarrow CH_2{=}CH{-}OCOR + HgCl_2.$$

Their behavior toward triphenylmethane halide, the reactions with which may proceed with formation of both C-derivatives and O-derivatives, depends on the nature of the halogen compound:



Since the mercury atom in these substances is connected to the carbon, it is necessary to recognize that for formation of the O-derivatives, the reaction proceeds with transfer of the reaction center in the examples given:



and the cause of the dual reaction appears to be not the tautomeric equilibrium, but the presence of the conjugated 1–2 and 3–4 bonds: ClHg–C=C–C=O.

This case differs from the preceding one, in that here both the keto and enol derivatives arise from the keto form. An appropriate scheme is:

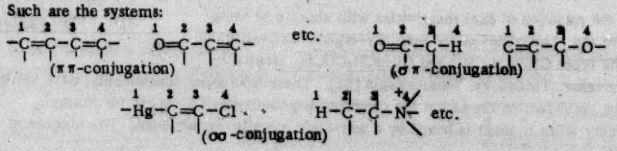
[No B]

(Scheme 2b)

Thus, the presence of tautomeric equilibrium does not appear to be an indispensable condition for the appearance of dual reactivity. The phenomenon of dual reactivity is also more widely distributed than is tautomeric equilibrium. In many cases, it was connected with tautomerism – real or simulated. However, in a considerably large number of cases, dual reactivity is observed for objects which are impossible to regard as being cases of equilibrium isomerism. It follows from the data summarized in the present report, dual reactivity seems to be a general property of molecules having conjugated bonds. Since the most important and widely distributed forms of tautomerism relate to substances the molecules of which contain a system of conjugated bonds, to that extent their dual reactivity seems to be a special case and and is related to this peculiarity of their structure. We consider this series of problems in more detail.

Systems of atoms (1–2–3–4...,) with conjugated bonds in the molecule differ in their capacities to react with the attacking reagent XY (and also with the ion or radical of X and Y) so that addition of the X molecules to the first atom of the system brings about a severance not only of the 1–2 bond, but also of the 3–4 bond, and the establishment of a new 2–3 π-bond. Often, but not without fail, in addition to that, the molecule Y adds to the fourth atom.

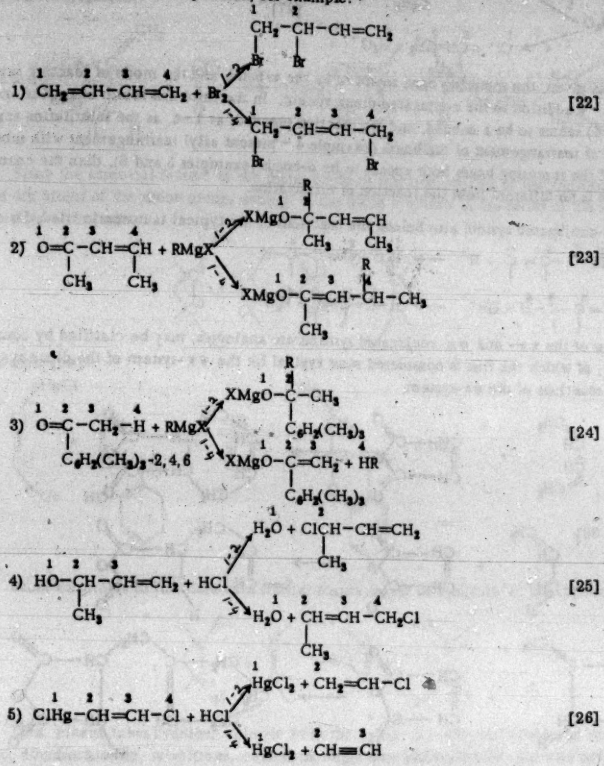
Such are the systems:



To the σσ-conjugation belong many quasi-complex compounds studied by Nesmeyanov, Freidlina, Borisov and their co-workers (see Bull. Acad. Sci., Div. Chem. Sci., beginning with 1940).

The reactivity of a system of such a type is characterized by the fact that reaction proceeds not only on the

1–2 bond, but also in the 1–4 position, for example: •



1) $CH_2=CH-CH=CH_2 + Br_2$ → $CH_2(Br)-CH(Br)-CH=CH_2$ (1–2) and $CH_2(Br)-CH=CH-CH_2(Br)$ (1–4) [22]

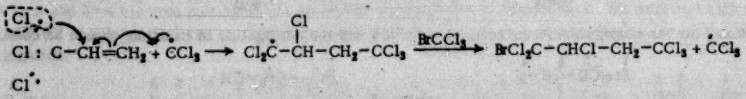
2) $O=C(CH_3)-CH=CH(CH_3) + RMgX$ → $XMgO-C(R)(CH_3)-CH=CH(CH_3)$ (1–2) and $XMgO-C(CH_3)=CH-CH(R)-CH_3$ (1–4) [23]

3) $O=C(C_6H_3(CH_3)_3\text{-}2,4,6)-CH_2-H + RMgX$ → $XMgO-C(R)(C_6H_3(CH_3)_3)-CH_3$ (1–2) and $XMgO-C(C_6H_3(CH_3)_3)=CH_2 + HR$ (1–4) [24]

4) $HO-CH(CH_3)-CH=CH_2 + HCl$ → $H_2O + ClCH(CH_3)-CH=CH_2$ (1–2) and $H_2O + CH=CH-CH_2Cl$ (1–4) [25]

5) $ClHg-CH=CH-Cl + HCl$ → $HgCl_2 + CH_2=CH-Cl$ (1–2) and $HgCl_2 + CH\equiv CH$ (1–4) [26]

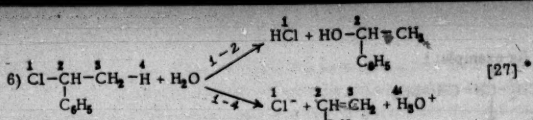
• In the present report we consider only the heterolytic reactions of the conjugated system. For homolytic reactions of the latter, which also are possible in the 1–2 and 1–4 positions, the process is induced by reagents of the radical type, and rupture and formation of new bonds are achieved not heterolytically, as in all the examples given here, but homolytically (see the articles by Nesmeyanov in the Sci. Reports of Moscow State Univ. for 1950) [20], and the book by Baker, "Hyperconjugation" – 1952 [28]. After presenting part of the usual phenomenon of tautomerism and the phenomenon mistaken for tautomerism (transfer of reaction center), accomplished as heterolytic reactions, we center our attention in the present report only on them. Then, in homolytic reactions there may appear not only π-, but also σ-conjugation, which is shown by the specificity of allyl brominations (for example, bromosuccinamide) or oxidations; Nesmeyanov, Freidlina and Zakharkin [29] also recently studied the rearrangement in the addition reactions of the $\dot{C}Cl_3$ radical or the Br atom to trichloropropylene:



$Cl : C-CH=CH_2 + \dot{C}Cl_3 \longrightarrow Cl_2\dot{C}-CH(Cl)-CH_2-CCl_3 \xrightarrow{BrCCl_3} BrCl_2C-CHCl-CH_2-CCl_3 + \dot{C}Cl_3$

$Cl^{\bullet}$

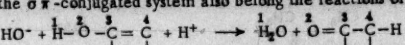
The homolytic reaction of the conjugated system considered will be the subject of a separate report.



[27] *

In the first two examples given, the rupturing bond seems to be the π-bond, and the mode of reacting seems to be that of the well known 1 – 4 addition to the conjugated diene system. In the third and fourth examples one of the rupturing bonds (1 – 2 or 3 – 4) seems to be a σ-bond, and the reaction proceeds at 1–4, as the substitution reaction of the conjugated allyl type of rearrangement of the bonds (example 4 – present allyl rearrangement with substitution of hydroxyl by chloride). If the rupturing bonds both appear to be σ-bonds (examples 5 and 6), then the course of the reaction in the 1–4 position is no different from the reaction of elimination.

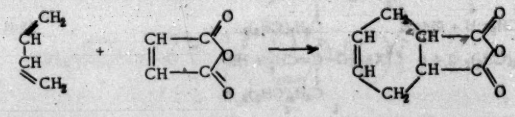
To reactions of the σ π-conjugated system also belong the reactions of the typical tautomeric triad, for example:



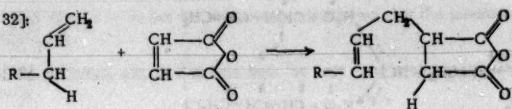
or

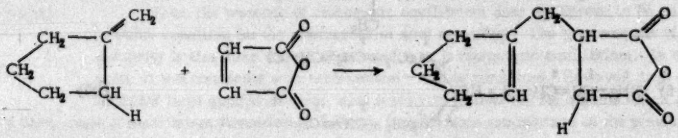
To what extent reactions of the π π- and σ π-conjugated systems are analogies, may be clarified by comparison of the reactions given below, of which the first is considered most typical for the π π-system of the diene synthesis, and the second is similar to reactions of the σ π-system:

I. π π-Conjugation:

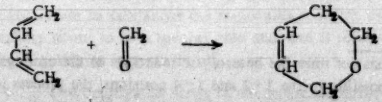


σ π-conjugation [31, 32]:





II. π π-conjugation [33]:

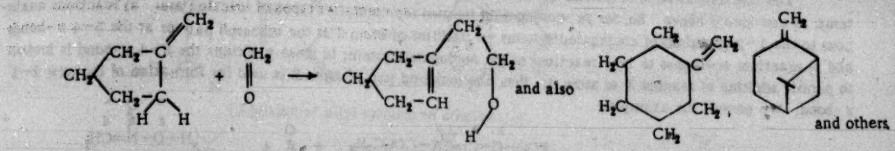


* In the schemes given, and also, like many others developed in the present report, we do not deal with the reaction mechanism in the sense of the orders of the separate elementary steps. With respect to the structures of the molecules having conjugated bonds, because of the nature of the reagent, the conditions of the medium, etc., the order of the reaction with the XY reagent or the molecules X and Y might be different. Particularly, for reactions of the type of (6), it is possible that the first step appears as an ionization also at the α-hydrogen; (see [30]):

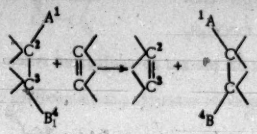
and essentially not the conjugation in the original molecule, but the conjugation in its anion, should be considered:

which, obviously, does not change the situation.

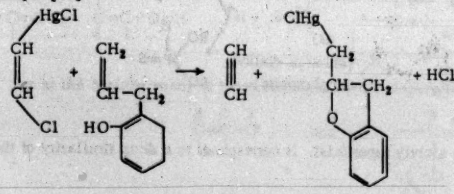
$\sigma\pi$-conjugation:



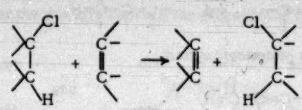
Since the essential feature of the diene synthesis reaction consists of the addition of an olefinic group to the 1st and 4th atoms of the diene group, analogs of the diene synthesis in the series of the $\sigma\sigma$-conjugated system should be reactions of the type:



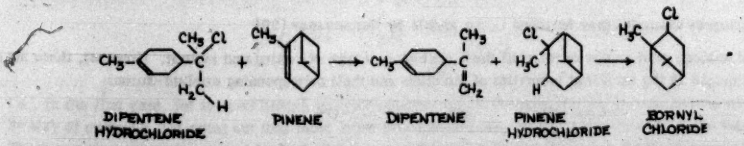
For example [34]:



Other examples of reactions of a similar nature might be reactions of the type studied by Aschan [35]:

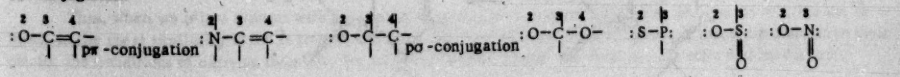


Thus, pinene takes hydrogen chloride from the mono- and dihydrochlorides of the terpenes (from the dipentene, dihydrochloride, sylvestrene, camphene, dipentene hydrochloride, and also hydrogen bromide from camphene hydrobromide, etc.), and is thus converted to bornyl chloride, for example:



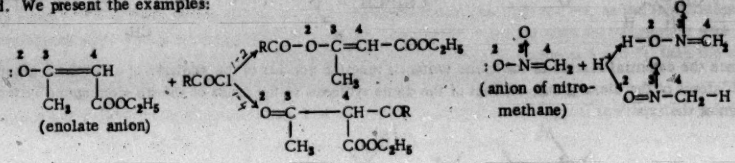
Naturally, such types of reactions are rare. They may be carried out only with strongly expressed $\sigma\sigma$-conjugations and an extremely active olefinic component.

As we shall demonstrate below, ... the thoroughgoing analogy of the preceding reactions, according to the nature of the reactions of such systems, in which one or both end atoms* are absent from the conjugated chain, and the 1–2 and 3–4 electron pair bonds act as the free electron pair of atoms 2 or 3. We shall call such a type of conjugation, p-conjugation, and in individual cases, shall designate it as: $p\pi$-conjugation, $p\sigma$-conjugation and pp-conjugation:

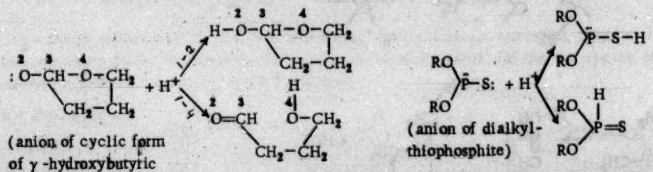


* Correspondingly, in the shcemes given below the numbering of the atoms begins with the 2nd.

The reactivities of such systems are characterized by the properties relating these systems to conjugated systems, as considered above. So, for pπ-conjugation the two representative types of reaction are: a) reactions analogous to the 1–2-reactions of conjugated systems — addition of atom 2 at the unshared pair or at the 3–4 π-bond; and b) reactions analogous to 1–4-reactions of the conjugated system; in these reactions the 3–4 π-bond is broken to permit addition of reagent X to atom 4; thus, the unshared pair of atom 2 is used for formation of the new 2–2 π-bond. We present the examples:

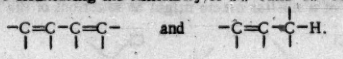


Similarly, two types of reaction exist also for the pσ-and pp-conjugated system

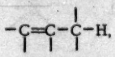


The analogy given does not appear to be merely superficial. It corresponds to a deep similarity of the chemical properties of conjugated systems.

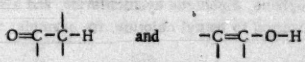
Examples were given above illustrating the similarity of ππ-and σπ-conjugated systems, for example:



It is well known that the three-carbon prototropic system

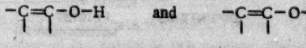


in many reactions is similar to the keto-enol triad



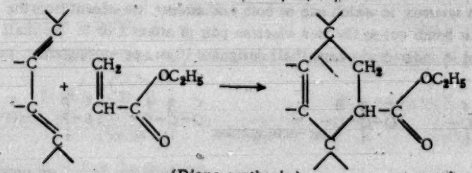
Many analogous examples may be found in the article by Nesmeyanov [20].

The bond analogy permits one to refer all these systems to a type of conjugated system. However, there are no differences in principle in the chemical properties of the enols and their corresponding enolate-anions:

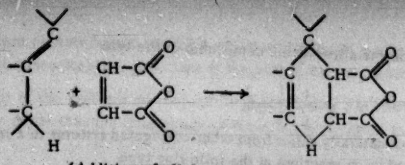


which refer to the pπ-conjugation type. Then, the fact that these latter systems actually behave as conjugated, is demonstrated by comparison of the Michael reactions (3) typical of them with the diene synthesis (1) and with the addition reactions given above for the system for a typical dienophile (2):

1)

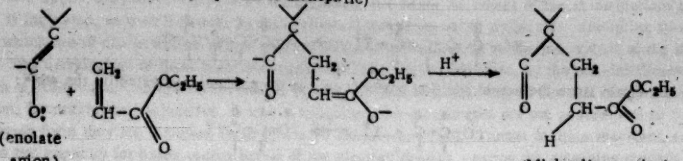


2)



(Addition of allyl systems to dienophile)

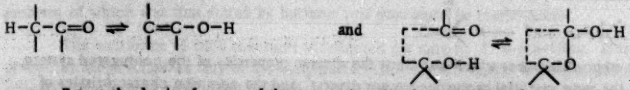
3)



(enolate anion)

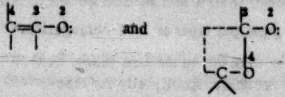
(Michael's reaction)

It is not necessary to demonstrate the existence of an analogy for the reactions of the keto-enols and cyclocarbonylic tautomeric systems:



and

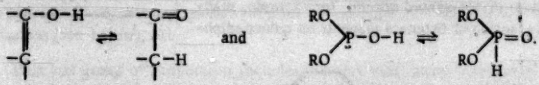
But at the basis of many of these reactions lie the properties of the anions



and

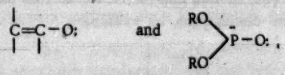
in the first case, for systems having $p\pi$-conjugation, and in the second – for systems having $p\sigma$-conjugation.

Finally, let us consider the analogy between the properties of typical keto-enol tautomeric substances and the dialkylphosphites:



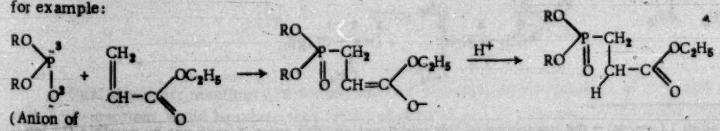
and

This analogy was first observed and substantiated in detail by A. E. Arbuzov [36]. Actually, it is easy to see the remarkable resemblance of the reactions of sodium diethylphosphite and of sodium derivatives of, for example, ethyl acetoacetate. However, at the basis of the reactions of these salts lie the properties of the corresponding anions



and

i.e., in the first case, for systems having $p\pi$-conjugation, and in the second – for systems having $p\rho$-conjugations. By way of example, we point out that these latter systems have the capacity for reactions of the Michael type. These reactions were discovered by B. A. Arbuzov and Pudovik [37] and studied in detail in numerous instances, for example:

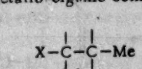


(Anion of dialkylphosphite)

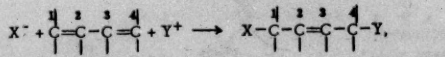
Thus, when we relate systems with p-conjugation to a type of conjugated system, we base the relation not so much on the great similarity of the reactions, but above all – on the profound similarities of many reactions as to their results, the conditions of carrying them out, the nature of reagent acting, the catalysts, the effects of media, etc.

Obviously, among conjugated systems of different types, diversities also exist. Thus, σ-conjugation, thanks to the smaller polarizability of the σ-bond in comparison to π-bonds, is as a rule expressed less strongly. A $\sigma\sigma$-conjugation requires substantial difference in the electronegativity of atoms A and B in the system

To the greatest degree this is observed in metallo-organic compounds of the type

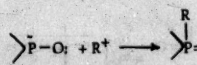


Furthermore, p-conjugated systems naturally differ from other conjugated systems in a number of properties. Thus, their 1−4 reactions are not 1−4 addition reactions of the following type:



do not appear since the actual addition proceeds only in the position, equivalent to the 4th*:

Accordingly, reactions analogous to the 1−4 reactions, for pp-conjugated systems limit their addition to one of two atoms of the diad (equivalent to the 2nd or 3rd atom of the 1−2−3−4 system):



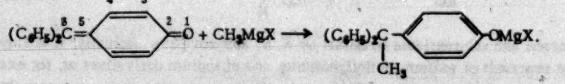
It is possible to present other differences which also limit the diverse properties of the conjugated system. In the present report, however, the most essential properties are not diverse, and the common characteristics of these systems permit us to consider them objectively from one general point of view.

In the following table are data of the principal types of 1−4-conjugation.**

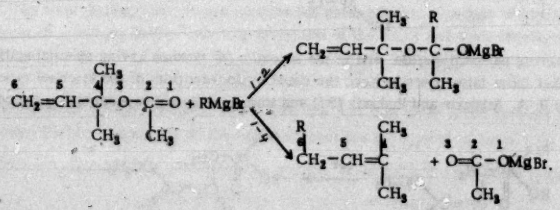
Any conjugated system has the capacity to react, in the first place, non-specifically for systems of 1−2-reactions and, secondly, specifically for reactions of the 1−4-type.

= − − =	ππ
− − =	σπ
− − −	σσ
= − :	πp
− − :	σp
: − :	pp

Besides conjugation of the usual 1−4-type, there are also conjugated systems which contain a large number of atoms in the chain (six, eight, etc). Accordingly, there are also 1−6, 1−8, etc., reactions of conjugated systems, for example, reactions of vinyl crotonic aldehyde or the action of Grignard reagents on quinonediphenylmethane [38]:



Nesmeyanov, Freidlina and Kochetkov [39] showed that for 1−6-reactions there is a capacity of the system not only for πππ-conjugation, but also for πσπ-conjugation, for example:



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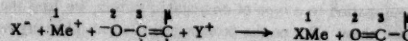
* In this reaction, atom 1 (absent) − the compound of this metal cation with anion Y may not be possible (in ionizing media) in accordance with the reaction



** The problem of the relationship of the assumed σ-conjugation and hyperconjugation was discussed in an article by Nesmeyanov [20].

However, for the system containing six and more atoms connected by conjugated bonds, the 1−2 and 1−4 reactions appear to be the most characteristic. Reactions at the ends of the conjugated systems occur more rarely.

The statement of the problem on conjugation given above, was presented according to its chemical characteristics. There is no doubt that the interaction of the valence electrons is of the essence of the relationships of conjugation.

This interaction, appearing most clearly for $\pi\pi$-conjugation, and being the object of the investigations of quantum chemistry, is indicated, as is well known, by many physical properties of the molecule: absorption spectra, the intensity of which are of characteristic Raman spectral frequencies, molecular refraction, values of the dipole moments, etc. The carrying out of these reactions requires definite steric conditions, by the non-fulfillment of which conjugation is eliminated. Such, for example, is the requirement of parallelism of the axis of the clouds of p- (or π-) electrons for maximum conjugation. For σ-conjugation, these conditions are not generalized to a sufficient degree. In rough form they are discussed in an article by Nesmeyanov [20]. Thanks to these reactions, conjugated systems have the capacity for easier redistribution of the electron density, causing the attacking reagent also to diffuse either to all or to part of the conjugated chain, depending on the nature of the attacking reagent and the conditions of attack. Hence – there are two or several directions of reaction. This is also one of the most important cases of the appearance of mutual effects which are not directly connected with the atoms in the molecule, the problem of which was first stated by Butlerov and developed by Markovnikov.

The existence of such reactions is reflected not only in 1−4-reactions. It is possible to verify the presence of special reactivities for any of the conjugated systems given above, as they differ from those for non-conjugated systems. Thus, e.g., a very well known extensive series of specific reactions of the conjugated dienes ($\pi\pi$-conjugation) are usually not characteristic of the olefins, such as a large number of reactions of the diene synthesis type, reactions with alkali metals, etc.

Reactions which may serve as examples of specific reactions of the $\sigma\pi$-conjugated system which do not appear as 1−4-reactions, are the deutero-exchange of α-hydrogen atoms in oxo-compounds and the allylic hydrogen in the olefins [40], and furthermore – the whole extensive range of directed reactions of the methyl (and homologous) groups with the benzene nucleus (oriented substitution) and the olefinic double bond (Markovnikov addition), and other phenomena considered in a series of articles and books on hyperconjugation (see, for example, the reports of Baker [28], Deasy [42]), for $\sigma\sigma$-conjugated systems, for example, the increasing facility of metal exchange in the chlorovinyl metal-organic compounds [41]; for $p\pi$-conjugation – there is the capacity of the enolate-anions for azo-combinations (see below), etc.

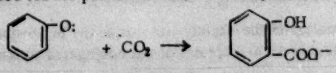
This last group of phenomena includes the very well known reaction of the 1st type orientants with aromatic nucleus, which results from the $p\pi$-conjugation of the free electron pair of the key atom of the orientant. Finally both series of phenomena are not only closely related, but seem to be different manifestations of the same conjugations. This is especially descriptively demonstrated by the examples given below. Thus, with respect to the phenolate ion (A)*, discussed below, for example, in the system of 2−3−4-conjugation (or 2−3−4−5−6, if we have in mind

(A)

and also the para-position) atom 2 has a free pair of electrons.

The 1−2-reactions will correspond to reactions of addition through free electron pairs with transformation of this free pair to a new σ-bond, for example, by the action of CO_2 on sodium phenolate with formation of salts of phenylcarbonic acid:

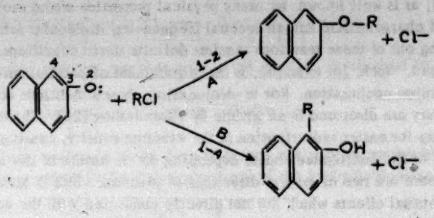
Dual reactivity, manifested in the present case as always by the existence of 1−4-type reactions together with 1−2-reactions, would be represented for the phenolate-ion, for example, by the Kolbe reaction:



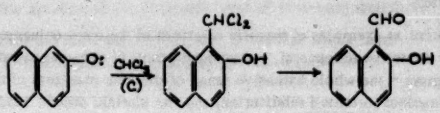
* We use the Kekule formula of the aromatic ring, naturally taking into account the adjusting of the π-bond of benzene and its disruption of its substituents. For the discussion of the material of the present report no formula of the benzene derivatives with adjusted π-bonds has preference over the Kekule formula.

The Kolbe reaction appears to be an ordinary reaction of electrophilic substitution into the aromatic nucleus, directed orientation of the 1st type, i.e., the specified $p\pi$-conjugation; therefore, we also designate this example as a typical case of ortho-para-orientation of electrophilic substitution into the aromatic ring.

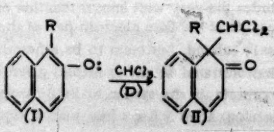
The question arises, on what basis do the authors compare the discussed types of reaction with the 1–4-reaction of the conjugated system? The sequence of reactions of the aromatic nucleus, presented below, containing an orientant of the 1st type, illustrates this.



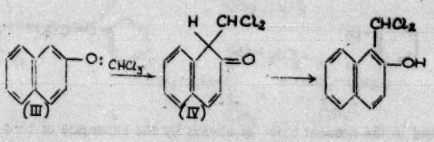
Alkylation of sodium β-naphtholate leads either to the alkyl ether of β-naphthol (1–2-reaction), or to α-alkyl-β-naphthol. A special case of the latter reaction – the alkylation of the nucleus – appears to be the Reimer-Tiemann reaction:



Comparison of the latter with the reaction [43]

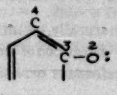


convinces us that they are essentially identical, and the single difference between reactions (D) and (C) appears to be the impossibility of returning to the aromatic form by way of enolization, which also is determined by the ortho-quinoid stage of the substitution reaction. Reaction (C) proceeds, obviously, entirely analogous to the mechanism

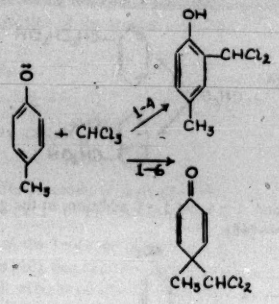


but is not determined by the ortho-quinoid stage, understandably.

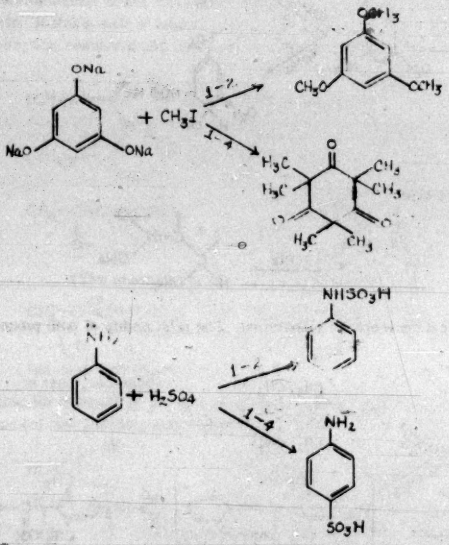
Meanwhile, the transformation of the naphtholate-ion to the ortho-quinoid derivative (II) or, correspondingly, to (IV), appears to be typical of 1–4-reactions of the conjugated system



The entirely analogous behavior of sodium para-cresolate in its reaction is of the dual type [44]:



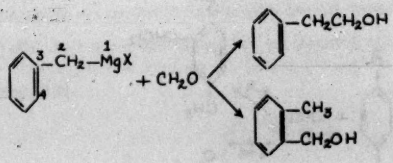
We present more examples [45]:



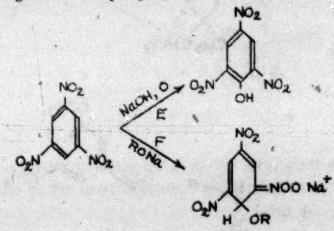
In many cases, it is difficult to distinguish between $p\pi$-conjugation and $\sigma\pi$-conjugations. In the metal phenolate when the O—Me bond is ionized, we class the substitution reactions for the phenolate nucleus with reactions promoted by $p\pi$-conjugation, as was stated in the above-mentioned examples. If phenolate reacts with the covalent O—Me bond, then such a type of substitution reaction into the aromatic nucleus will belong to the reactions of directed $\sigma\pi$-conjugation.

The reaction of benzylmagnesium halide with oxo-compounds may serve as the next step in this series of reactions: (see diagram at top of next page), where the C—Mg bond is covalent and, consequently proceeds on $\sigma\pi$-conjugation.

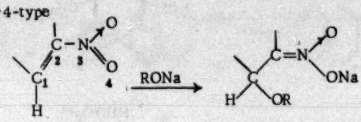
As for orientation of the nucleophilic substituent in the aromatic nucleus, directed by orientants of the 2nd type, in these cases the matter at issue are chiefly $\pi\pi$-conjugations, while the circumstances explaining the



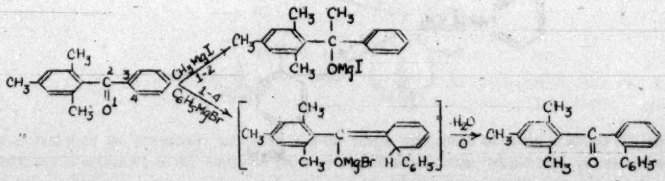
analogy of the usual nucleophilic substitution and 1 – 4 and 1 – 6 addition, in the given case arise in a manner completely analogous to the foregoing. For example [46]:

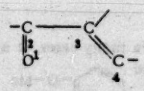


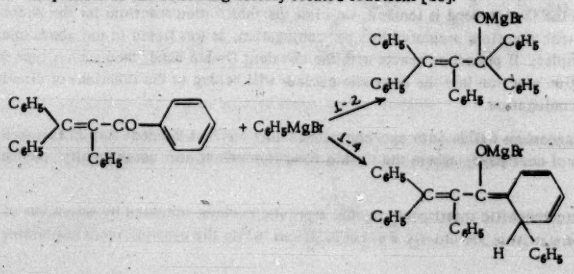
Reaction (F) belongs to the 1–4-type



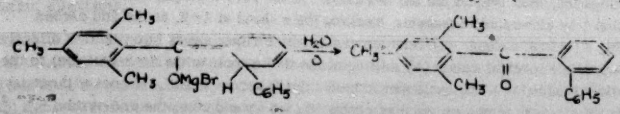
Reaction (E) – is a typical nucleophilic substitution. The relationship of both processes is definite. Another example [47]:



Whenever ortho-phenylation appears as a 1–4-reaction of the conjugated system  it proves comparable to the following closely related reactions [48]:

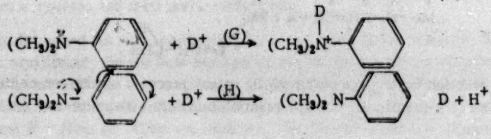


The structure of the latter brightly colored polyene product of 1–4-addition was accurately substantiated. This instance differs from the preceding reaction of ortho-phenylation of the benzomesitylene only in the impracticability of the latter stage-reduction of the aromatic system:

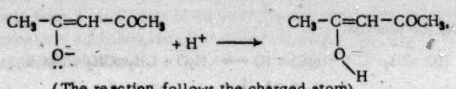


All this permits us to refer processes of aromatic substitution to the type of reactions of the conjugated system closely related to the 1–4- (or 1–6- for para-position) reactions.

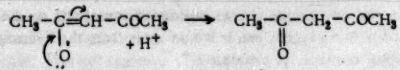
In any of the examples of the 1–4-type of reactions given on pp. 43-44, we may consider, in accordance with the assumption of one of us [20], that the reactions proceed with transfer of reaction center. These conjugated systems may give reactions both without transfer of reaction center (1–2 reactions), and with transfer of reaction center (1–4 or 1–6 reactions). Thus, in the case of the presence in the molecule of an atom with a free p-pair, this atom is the usual reaction center of the molecule; at the expense of the capacity of the p-pairs to combine with nucleophilic reagents. If this p-pair is conjugated, for example, with π-bonds, then, besides the normal reactions of addition at the reaction centers of (G), reactions are possible with its transfer (H) in accordance with the scheme [49]:



Another example:

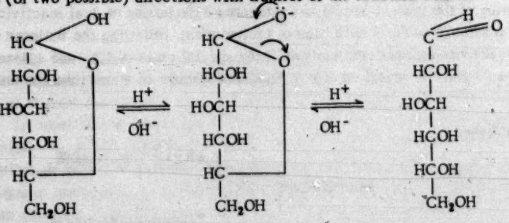


(The reaction follows the charged atom)



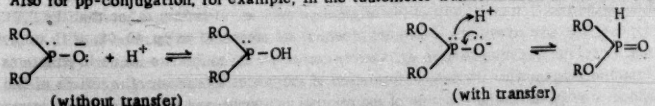
(Reaction with transfer of reaction center)

For po-conjugation, for example in the process of mutarotation of glucose, addition of a proton to the glucose anion proceeds in one (of two possible) directions with transfer of the reaction center:



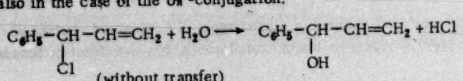
(without transfer of reaction center) (with transfer of reaction center)

Also for pp-conjugation, for example, in the tautomeric transformation of the dialkylphosphites

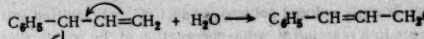


(without transfer) (with transfer)

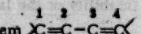
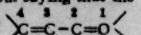
Things are analogous also in the case of the σπ-conjugation.



(without transfer)

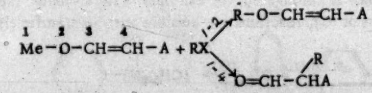


(with transfer)

For $\pi\pi$-conjugation, most typical are the two cases: in the first, a conjugated diene system  is attacked at position 1 by electrophilic reagents, breaking the π-bond at 1–2, at the 2nd carbon atom, and developing a positive carbon -ene reaction center which either enters into reaction directly, or results in transfer of the carbon-ene reaction center (by shifting of the 3–4 π-pair to the 2–3-position) to the 4th carbon atom, where the action of addition of the nucleophilic molecules is accomplished. It goes without saying that the present scheme does not claim to report the order of events. In the second case, the ene-system  and its similar $\pi\pi$-conjugated system is subjected to the attack of nucleophilic molecules already having, at position 2, a positive reaction center in the form of the carbonyl carbon. Thus, the 1–2-reaction proceeds. In case of the 1–4-reactions, attack is undergone at the 4th carbon atom, which consequently transfers the reaction center from the 2nd carbon atom to the 2–3-position, by means of a shift of the π-pair at 3–4, and breaking of the π-bond of the carbonyl group, with removal of the p-pair to oxygen.

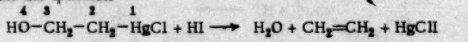
In a similar way, the reaction center also is transferred for $\sigma\pi$- and $\sigma\sigma$-conjugations.

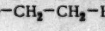
In the case, for example, of the reaction



without transfer of the reaction center, the electrophilic attack proceeds on the one center of electrophilic substitution – the oxygen atom (1,2-reaction). The 1,4-reaction proceeds with transfer of the nucleophilic reaction center to the 4th carbon atom.

It is the same also for the reaction

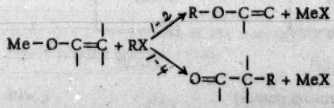


where the 1st atom of the conjugated system  undergoes nucleophilic attack; as a result, the mercury cation is broken away from the carbon, and the anionic charge, instead of remaining on the 2nd atom of the conjugated system – carbon, is transferred to the fourth – oxygen, and it breaks away from the hydroxyl anion – a new nucleophilic center, capable of absorbing electrophilic attack, for example H^+.

Thus, these are reactions with transfer of reaction center – these are 1–4-reactions of conjugated systems (and, it is understood, 1–6-, etc.).

At the beginning of the present article, we presented a definition of dual reactivity in such a form, that isomeric equilibrium was substituted for a definition of tautomerism, following the Butlerov concept. Obviously, such a definition of dual reactivity agrees completely with the special cases of 1,2- and 1,4-reactions of conjugated systems, expressly with 1,2- and 1,4-reactions of σ-conjugated systems of atoms (and the corresponding p-conjugated system).

Thus, the reactions



seem also to be simultaneously reactions of the 1,2- and 1,4-type, and reactions forming derivatives (specifically substituted ones) corresponding to the two isomeric forms of the original compound. It is easy to see that the 1,2- and 1,4-reactions of other types of conjugated systems, examples of which are presented on pp. 43-44, still are not covered by the definition of dual reactivity, the capacity to form derivatives corresponding to the two isomeric structures of the original substance. Meanwhile, apparently, any case of formation of substances as a result of reactions of two series of derivatives, one of which corresponds to the structure of the original substance, and the other – to its isomer, may be interpreted as the result of 1–2 or 1–4-type reactions of the conjugated bond systems of the original substance.

Introduction of the profound analogy of all the types of conjugated systems as to their capacities to react dually according to the 1,2- and 1,4-types, as demonstrated above, has the effect of broadening the concept of dual

reactivity. Dual reactivity also should be considered as a capacity of the compounds to react according to the 1,2- and 1,4- (and accordingly the 1,6- etc.) type. Such a capacity, as was discussed above, is characteristic of molecules with conjugated bonds. Hence, it is clear that in the concept brought out by the authors' report, the dual (triple, etc.) reactivity of a compound is by no means identical with the capacity of any substance to react generally in different directions.

However, we return to the problem of the reactivity of tautomeric substances. In the reports cited above it was shown that in metallic derivatives of the keto-enol system, the capacity for dual reactions with formation of both keto and enol derivatives was not related to tautomeric equilibrium: One single form, for example a metal enolate, had the capacity to react in two directions, forming both series of derivatives. We expressed the assumption that such a matter also holds for the metallic derivatives of other tautomeric systems, for example, the lactim-lactam system. In the latter, both the anion and the metal derivative, obviously, have the lactim form, but also have the capacity to react with alkylating and similar agents, forming both lactim and lactam derivatives.

Thus, there is created an apparent sharp internal contradiction between the metal derivatives of a tautomeric system and the system itself (i.e. hydrogen derivatives). For the first, the possibility of a dual reaction without tautomerism was shown; the second continued to be the current point of view of explaining the dual reactions of tautomeric systems by the presence of tautomeric equilibria of two forms, each of which was responsible for one of the directions of reaction. The present report eliminates this apparent contradiction and shows that the situation is identical both in tautomeric systems and their metal-derivatives.

The next question to be posed in this connection is: what is the origin of the dual reactions in the presence of tautomeric equilibria? Do the keto derivatives always arise from the keto forms, and the enol derivatives — from the enol form? Or — in a general way: if there is equilibrium of $A \rightleftharpoons B$, and as a result of different reactions the equilibrium mixture forms derivatives A' and B', then what is the basis for assuming that A' forms directly from A and B' — from B? Once we know that, for the derivatives of the A' and B' type, one may form only from A, or one only from B, as a result of the reactions occurring with and without transfer of reaction center in the absence of tautomeric equilibria, then it is natural to assume that also in the presence of tautomerism, we do not exclude similar types of behavior.

The first case, which must be considered is — this reaction capacity of tautomeric substances with strongly displaced tautomeric equilibria. The concentration of one of the forms, thus, is very small (case of "pseudomerism"). If the equilibrium, $A \rightleftharpoons B$, is displaced in the direction of A (equilibrium constant $K_T \ll 1$), then the formation of A' from A, in principle, does not represent an exception. However, a very strongly displaced equilibrium formation of B' from B, at extremely small concentrations of B, is not always possible. As shown by Kabachnik [50], the transformation of the equilibrium mixture $A \rightleftharpoons B'$ by the scheme of pseudomeric transformation:

$$A \underset{k_2}{\overset{k_1}{\rightleftharpoons}} B \xrightarrow{k_3} B' \quad (K_T = k_1/k_2)$$

always runs more slowly than by direct transformation of $A \longrightarrow B'$, with the same initial concentration and with the rate constant, k', diminished, in contrast to that observed, by $1/K_T$ times. If K_T is always small (below 10^{-10}) then the rate of formation of B' from the mixture $A \rightleftharpoons B$ through B, is extremdy small (according to the smallness of the concentration of B). In order for the formation of B' fromB to proceed at a tangibly observable rate, it is necessary for the rate constant, k_3, of the reaction $B \longrightarrow B'$ to be unusually large (of the order of 10^{10}–12^{12} sec^{-1} for a unimolecular transformation, or 10^{10}–10^{11} $l.mole^{-1} sec^{-1}$ for a bimolecular). But rate constants of such an order are not characteristic of organic molecules. It is known that only ions or radicals (or atoms) have the capacity to react with so great a rate constant. Consequently, with the tautomeric equilibrium of $A \rightleftharpoons B$ strongly displaced to the side of A ($K_T \leqslant 10^{-10}$), the formation of B' from B is not realized practically.

The hypothesis of pseudomerism, introduced at the end of the last century, when the techniques of measuring strongly displaced equilibria were still very poor and comparatively little was known about the rates of chemical reactions, contradicts the facts. If the equilibrium of $A \rightleftharpoons B$ is not strongly displaced, then it appears to be an ordinary tautomeric equilibrium (below the limit of K_T of the order of 10^{-4}–10^{-5}), the concentration of the B form is entirely measurable, its presence may always be demonstrated, and there is no basis for separating this equilibrium from the general system of tautomeric equilibria. If the same equilibrium is displaced more strongly to the side of A, then the formation of a derivative B' from B, at practically observable rates, becomes impossible. Consequently, we do not abandon our position on the hypothesis of pseudomerism.

Here it is necessary to point out two important limitations. After publication of the demonstration [50, 51]

cited above, objections, based on incorrect understanding of what was discussed, were repeatedly expressed. In this demonstration, nothing denied the possibility of the existence of strongly displaced equilibria. Such equilibria, undoubtedly, exist. As was shown by Kabachnik [52], the tautomeric equilibrium constant K_T was always equal to the ratios of the ionization constants (or protolysis constants) of the tautomeric forms in a given medium (S):

$$K_T = \frac{K_{1S}}{K_{2S}}.$$

For large differences in the ionization constant (acid or base), which may amount to 10^{14} or higher, the position of the equilibrium may accordingly be strongly displaced toward the side of the less acid (less basic) form. With the development of measuring techniques, better possibilities of measuring strongly displaced equilibria will appear. However, we maintain that for such strongly displaced equilibria of the reactions, the corresponding scheme of pseudomeric transition, $A \rightleftharpoons B \longrightarrow B'$, may not determine the actual observable course of the process.

Furthermore, in the reports cited, it was not maintained that it is generally impossible to have reactions with intermediate formation of reaction products, the concentration of which may be exceedingly small (below 10^{-6}–10^{-8} mole liter^{-1}). However, it was maintained that such particles may not be molecules (which corresponds to the idea of pseudomerism). These may be either radicals or ions, reacting often without energy of activation or with only a small energy of activation. In these cases the question at issue is not tautomeric (pseudomeric) equilibria, but equilibria of molecules with ions, or molecules with radicals, i.e., dissociation equilibria.

We explain this example. On the basis of the well known work of Lapworth and others on the halogenation of acetone in dilute aqueous solutions [53] (pseudounimolecular reaction) we took the point of view that the halogenation preceded enolization:

1) $CH_3-COCH_3 \underset{k_2}{\overset{k_1}{\rightleftharpoons}} CH_3-\underset{OH}{C}=CH_2$ (slow)

2) $CH_3-\underset{OH}{C}=CH_2 + I_2 \xrightarrow{k_3} CH_3-\underset{HO}{\overset{I}{C}}-CH_2I$ (fast)

3) $CH_3-\underset{HO}{\overset{I}{C}}-CH_2I \xrightarrow{k_4} HI + CH_3COCH_2I.$

Since the tautomeric equilibrium constant of acetone is now known and equals $2.5 \cdot 10^{-8}$, it is necessary to assume that the rate constant of the rapid stage 2 (pseudounimolecular) is considerably larger than $4 \cdot 10^5 \cdot k_1$.

The observed magnitude of the rate constant of the iodization of acetone by alkali catalysis is of the order of $>10^1$ sec.$^{-1}$. Hence, it follows that the order of magnitude of k_3 is 10^6–10^7 sec.$^{-1}$ or higher [54]. Magnitudes of this order are not very likely for neutral organic molecules, and consequently, the scheme given was not applicable to the reaction of iodization of acetone employing an alkaline catalyst.

Actually, the more recent investigators [55], arrived at the conclusion that the halogenation of acetone and other ketones proceeds in alkaline medium, not through the tautomeric enol form, but through the corresponding anion, forming directly from the keto form:

1) $CH_3COCH_3 + OH^- \underset{k_2}{\overset{k_1}{\rightleftharpoons}} CH_2=\underset{O^-}{C}-CH_3 + H_2O$ (slow)

2) $CH_2=\underset{O-}{C}-CH_2 + I_2 \xrightarrow{k_3} I-CH_2COCH_3 + I^-$ (fast)

The second step of the reaction, since it proceeds with the assistance not of the neutral molecule, as in the preceding case, but with ions, may be characterized by an extremely high rate constant.

On iodization of acetone in acid medium, the rate constants are of the order of 10^{-4} sec.$^{-1}$. The corresponding values for k_3 will have an order of 10^{+1} sec.$^{-1}$. It is possible to think that a rate constant of such an order is possible for the molecular enol forms. The reaction proceeds through the enol:

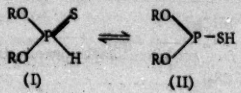
1) $CH_3COCH_3 + H_3O^+ \rightleftharpoons CH_3-\overset{OH}{\overset{|}{\overset{+}{C}}}-CH_3 + H_2O \overset{\text{slow}}{\rightleftharpoons} CH_3-\overset{OH}{\diagup}C=CH_2 + H_3O^+.$

and in this connection, consequently, the assumption of Lapworth is correct.

In what way does the dual reactivity of a tautomeric substance, with strongly displaced tautomeric equilibrium, arise? On the bases stated above, it is possible to assume that, for strongly displaced tautomeric equilibria, the dual reaction arises as a result of the course of the reaction according to two possible paths – with or without the transfer of reaction center. Derivatives of both series A and B arise from A, but not from B. An appropriate scheme is the following:

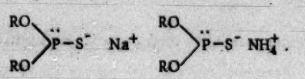
(Scheme 3)

It is possible to cite a large number of examples of reactions of similar type. To them belong the reactions of the dialkylthiophosphites, studied by Kabachnik and Mastrukov [51]. The tautomeric equilibrium of these substances is displaced, to a high degree, to the side of form (I). The presence of form (II) is observed neither in reac-

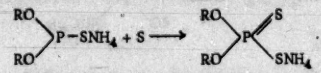


(I) (II)

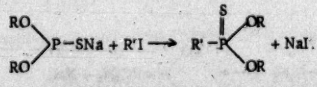
tions with sulfur, the addition of which is characteristic of derivatives of trivalent phosphorus, nor for reactions with the halogen salts of monovalent copper (which also is characteristic for P^{III}) nor finally, for reactions with alkyl halides. However, the dialkylthiophosphites have the capacity for forming sodium and ammonium salts, the structures of which are definite.



These salts easily add sulfur:



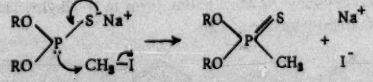
They are alkylated by alkyl halides with the formation of esters of the alkylphosphonothionic acids:



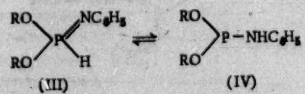
At the same time, these salts are easily hydrolyzed by water with the formation of the phosphite (I). This demonstrates the presence of the tautomeric equilibrium (I) $\rightleftharpoons$ (II), since the hydrolysis of the salt of such an equilibrium pair of acids should proceed as if it were the hydrolysis of the salt of the less acid form (I).

It is necessary to assume that the process of formation of salts of the dialkylthiophosphites proceeds with transfer of the reaction center, similar to the formation of salts of the keto enols from the keto forms:

In the same way, by transfer of the reaction center, the alkylation of the salts by reaction with alkyl halides proceeds thus:

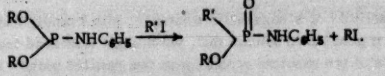


A different relationship was observed for the dialkylanilidophosphites, studied by Kabachnik and Gilyarov [56]:

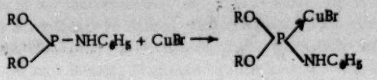


(III) (IV)

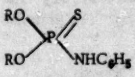
Here the equilibrium was displaced to the side of the forms having a tervalent phosphorus (III) atom, and the presence of form (IV) was observed in many characteristic reactions. As the derivatives of tervalent phosphorus, these substances have the capacity for the Arbuzov rearrangement:



They add the halide salts of monovalent copper:

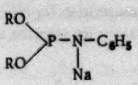


Finally, they add sulfur, resulting in the formation of the thioanilides of dialkylphosphoric acids:

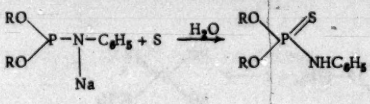


Together with reactions of the form (IV), free dialkylanilidophosphates also enter into reactions, characteristic for substances with a $\rangle P{=}N$ bond (action of CS_2).

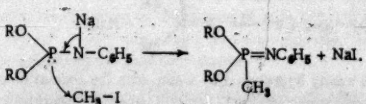
By the action of the alcoholates, the dialkylanilidophosphites form the salts:



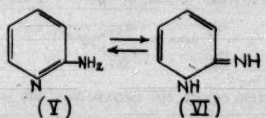
The structure of these salts was demonstrated by their capacity for addition of sulfur, with formation of the thioanilide salts



Salts of the dialkylanilidophosphites are alkylated by alkyl halides, differently from free dialkylanilidophosphites. The reaction proceeds with transfer of the reaction center and with the formation of derivatives having the form (III):

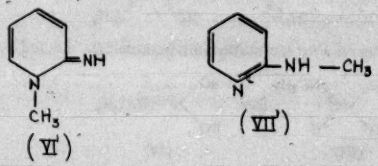


An extremely interesting example appears to be α-aminopyridine, studied in his time by Chichibabin [8]. For this substance, the characteristic dual reactivity was interpreted as an appearance of tautomerism:



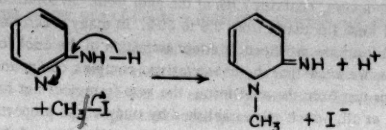
(V) (VI)

Thus, methylation of aminopyridine by alkyl halide leads to N-alkylpyridonimine (VI'), and methylation of its sodium salt – leads to methylaminopyridine (VII'):

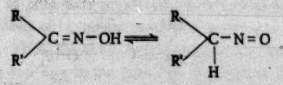


(VI') (VII')

Recently, Goldfarb and Setkina [57], on the basis of investigations of the absorption spectra of α-aminopyridine, showed that the content of form (VI) in the mixture, if it is present, is so small that it is not observed spectrally. Furthermore, the use of the so-called carbonate method, offering the possibility of finely distinguishing the aminopyridine structure from the pyridonimine, showed the virtual absence of the pyridonimine form [58]. It is necessary to assume that the formation of pyridonimine derivatives from α-aminopyridine proceeds not through the tautomeric form (VI), but directly from (V) with transfer of the reaction center:



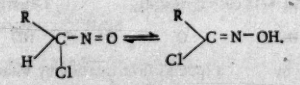
A good example of dual reactivity might be the reaction of the oximes of aldehydes and ketones. The tautomeric equilibria of these substances with the corresponding nitrosocompounds is displaced to a high degree in the direction of the oxime form. In all the reactions in which we should expect the formation of the nitroso-derivative, with the nitroso-group on the carbon atom connected with hydrogen (VIII), invariably only the oxime (VII) was obtained.



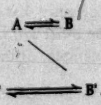
(VII) (VIII)

Not one case of isomerization of the oximes in nitroso-combination (the matter at issue is aliphatic nitroso-compounds) is known. Finally, the majority of reactions of the oximes correspond to the oxime form. However, upon halogenation of the oximes, halides of the nitroso-compounds are formed, which are slowly transformed into the corresponding acid halides of hydroxamic acid (if such a transformation is possible) [59]. It is possible to assume with assurance that the reactions of halogenation of oximes proceed with transfer of the reaction center:

For the aldoximes, it is accompanied by subsequent transformation to the chloranhydrids of hydroxamic acid:



The scheme of the dual reaction for this example should be written in the following form (A – the oxime, B – nitroso)



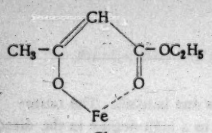
(Scheme 4)

Nitration of the oximes proceeds in a similar manner; it is complicated only by the subsequent oxidation of the nitroso-group [60].

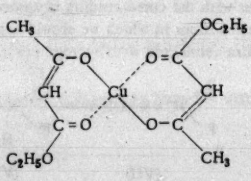
It is possible to cite more examples of a similar nature. Here belong the dual reactivities of α- and γ-pyridones, carbostyril, the amides of carboxylic acids and many others. In all these cases, it is possible to assume that the dual reactivity does not appear as a result of tautomerism, although all these substances are tautomers. The tautomeric equilibrium is strongly displaced to the side of one form, which also enters into the observed chemical reaction. Thanks to the presence of conjugated systems of bonds in it, , this form has the capacity for dual reactions. For the reactions, together with the derivatives corresponding to their structures, there also arise, as a result of the reaction with transfer of the reaction center, derivatives of the second form, and this creates the impression that both series of derivatives arose as a result of the tautomerism.

The last problem which must be considered in the present report relates to the reactivity of tautomeric substances, the equilibria of which are not displaced toward one side to a high degree. This is the most abundant form of tautomeric equilibria (β-dicarbonylic compounds, aliphatic nitro-compounds, nitrosophenol, the dialkylthiophosphates which we recently studied, etc.). All these substances are characterized by the presence of systems of conjugated bonds, thanks to which they have the capacity for reactions with transfer of the reaction center. On the other hand, the concentrations of both tautomeric forms, if not equal, are commensurate. Consequently, each of the forms has the capacity to enter into the reaction. Each of these two factors may be the cause of dual reactions.

Ethyl acetoacetate, as is well-known, contains 7.5% of the enol form. In solutions, depending on the nature of the solvent, the content of the enol form fluctuates from 0.5 to 50%. In many reactions in which derivatives of the enol form are produced, a direct transition of the enol form to its derivative occurs. Thus, we know that the characteristic complex compound with ferrous chloride (K) forms just from the enol form: the keto form does not have the capacity for this reaction at all, which was established by study of the properties of the pure keto form. The same holds true of the formation of the difficultly-soluble copper compound

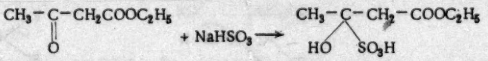


(K)

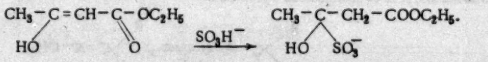


Rapid bromination was also characteristic of the enol form. It is known that the keto form reacts with bromine only very slowly.

However, when considering some other typical reactions of ethyl acetoacetate, it is not possible to take a definite stand. Thus, we consider that the formation of the bisulfite derivative is a characteristic reaction of the keto form:

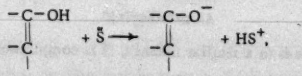


However, it is possible to conceive of formation of the bisulfite derivative also from the enol form. Thanks to the presence of conjugated multiple bonds with the ester carbonyl group, it can be assumed that the addition of bisulfite to the multiple bonds (as in acrolein) is feasible:

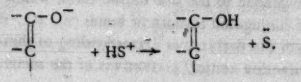


It is possible to determine, only by a special investigation by what method the bisulfite derivatives actually form. The same can be stated also for the formation of cyanohydrin, methylisoxazolone, phenylmethylpyrazolone, etc.. This problem is not yet clear.

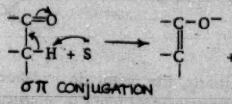
In a series of cases it is possible to prove with certainty that from one form, as a result of reaction with transfer of reaction center, there arises the derivative of the other form. First of all, this relates to the mechanism of the mutual transformation of the forms. Ionization, for example, of the enol form, proceeds like a 1-2-reaction:



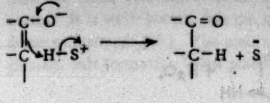
here $\ddot{S}$ is the protophilic solvent particle or any other base present in solution. Also the recombination of ions on the side of the enol form proceeds without transfer of reaction center; the proton is attached at the site of the anion charge, i.e., at the oxygen:



Ionization of the keto form leads to an anion having the enolate structure; the process proceeds with transfer of the reaction center (1-4):



Recombination of the ions on the side of the keto form also proceeds with transfer of the reaction center.



Thus, on the whole, the keto-enol transformation processes resemble a series of successive ionization and recombination reactions of two acids (ketone KH and enol EH), both forming generally the E^- anion, which can be expressed by the scheme:

$$KH + S \rightleftharpoons E^- + HS^+ \rightleftharpoons EH + S.$$

On this basis, Kabachnik [52] used for calculation of the tautomeric equilibria, the existing theory of acid-base equilibria, developed by Brönsted [61] and more recently – Izmailov [62].

The applicability of the theory of acid-base protolytic equilibria to tautomeric equilibria is confirmed by the scheme discussed above. On the basis of it, we succeeded in deriving a fundamental quantitative relationship, characterizing tautomeric equilibria. Thus, the tautomeric equilibrium constant, K_{TS} is equal to the ratio of the ionization constants of the forms K_{KS} and K_{ES} in the presence of medium, S:

$$K_{TS} = \frac{K_{KS}}{K_{ES}}.$$

It is possible to express, thermodynamically, the ionization constants K_K and K_E and the activity coefficients of the keto and enol forms:

$$K_{TS} = \frac{K_K}{K_E} \cdot \frac{f_{KS}}{f_{ES}},$$

The ratio of the thermodynamic constants, called by one of us "The thermodynamic constant of tautomeric equilibrium," does not depend on the nature of the solvent* and is characteristic of the "enolizability" of the keto-enol:

$$K_t = \frac{K_K}{K_E}.$$

The ratio of the activity coefficients f_{KS}/f_{ES} characterizes the effect of the solvent on the position of the equilibrium (enolizing capacity of the solvent).

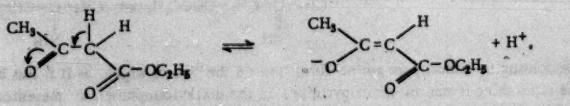
On the basis of these concepts, we developed the dependence of the tautomeric equilibrium constant on different media, S_1 and S_2:

$$pK_{TS_1} = pK_{TS_2} + \text{const}$$

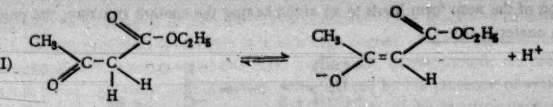
and, all things considered, the well-known formula of Meyer [63] $K_{TS} = EL$, which he found empirically [64].

Furthermore, as shown by Kabachnik and Ioffe [65], both tautomeric forms may be titrated in solution potentiometrically, and their ionization constants determined; thus, it was shown that for the ketones and enols, as for the acids, the well-known rule of acid-base equilibria, found for the common acids and bases, was applicable.

The concept of the ionization of the keto form with transfer of reaction center permits one to understand also the behavior of the cis- and trans-enol forms in solutions. If the process of removal of a proton from the keto form takes place with the reversal of the isomer (I), then there arises the cis-enol form. Fromthe reversed isomer (II), there arises the trans-enol form:

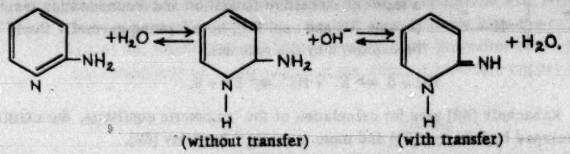
(I) 

*Assuming that all solvents are equally active, when reduced to normality.

(II) 

Applying the concept of tautomeric equilibria, like protolytic acid-base equilibria, we succeeded in elucidating the mechanism of the equilibrium of the cis-trans-enol forms in solutions and their relation to the nature of the solvent.

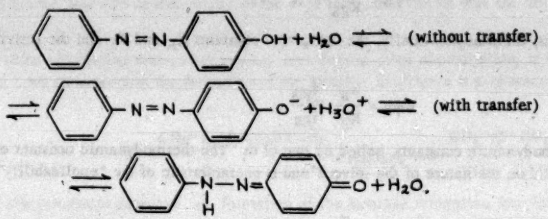
There is no doubt that also other tautomeric transformations, not of the keto-enol type, are connected with processes of transfer of the reaction center. Such a tautomer is α-aminopyridine.



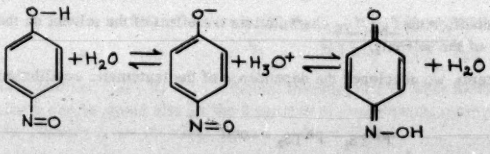
(without transfer) (with transfer)

Since pyridinoimine forms appear to be incomparably stronger bases than aminopyridine (the respective ionization constants of the methylated forms are of the order of 10^{-4} and 10^{-9}), then the equilibrium constant equals 10^{-5}. The equilibrium, as always, was displaced to the side of the less acid form, in the present case – toward aminopyridine (see below).

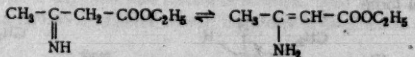
We present still another example: the tautomerism of azo-hydrazone



The tautomerism of nitrosophenol is:

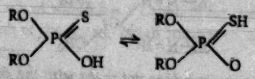


The position of the tautomeric equilibrium in all the cases depends on the relative basicity (or acidity) of the form in a given medium. Thus, the equilibrium, as follows from the formula given above, always is displaced to the side of the less basic (or, accordingly, less acid) form. Since the ratio of the ionization constants depends on the nature of the solvent, then the position of the tautomeric equilibrium also depends on the nature of the solvent. This relationship is expressed by the formula given. If one of the forms exceeds the other, according to the thermodynamic constant of ionization, the equilibrium in all solvents is displaced toward the side of the less ionized form. Thus, while ethyl acetoacetate at equilibrium contains 7.4% of the enol form, this percentage changes strongly with transition from one solvent to another, ethyl iminoacetoacetate



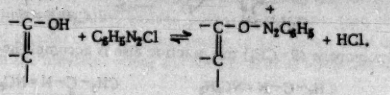
representing its almost pure amino-form, toward the side of which, as it is less basic, the equilibrium is displaced. The same thing is true for aminopyridine. In the dialkylthiophosphites presented above, the equilibrium is displaced to the side of the form with pentavalent phosphorus, as it is less acidic. For the dialkylanilidophosphites, the

equilibrium is displaced to the side of the tervalent form. In the investigations of Kabachnik, Ioffe and Mastrukov, the dialkylthiophosphates

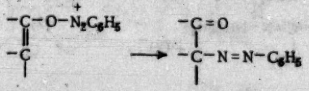


in equilibrium in aqueous or alcoholic solutions, contain both forms (ratios from 2:8 to 8:2), since their acid properties are close (ionization constants of the order of 10^{-2}–10^{-3}).

Besides the process of tautomeric transformation, it is possible to point out also other reactions for which, from one form, derivatives of the second form are produced, as a result of the reaction with transfer of the reaction center. It is well-known that the keto form of β-dicarbonylic compounds do not react at all with the aromatic diazo-compounds [66]. The enol form, on the contrary, readily reacts with the diazo-compounds; thus, in the beginning, salt formation takes place:



The diazoenolate forming readily rearranges to the azo-compound of the keto form:

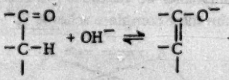


(and, if it is possible, further – to the hydrazone).

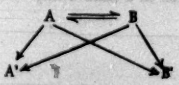
Thus, only the enolate enters into azo-coupling reactions, the reaction product having at once the ketonic structure. It is necessary to supplement the scheme of the reactivity of ethyl acetoacetate (which is a classical example of tautomerism) with the possibility of a direct transition of B → A':

(Scheme 5)

If we consider the fact that the alkali salts of ethyl acetoacetate, which are derivatives of the enol form, also arise directly from the keto form by the action of alkali

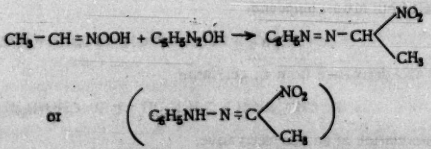


or by the ionization in neutral medium presented above, then the scheme of the reactivity of ethyl acetoacetate proves to be still more complex (6).

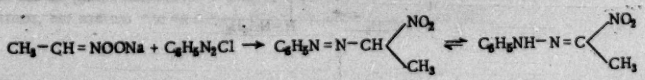


(Scheme 6)

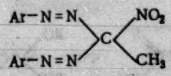
The aliphatic nitro-compounds, as is well-known, show a reactivity characteristic of both forms found at equilibrium. However, only one form reacts with the aromatic diazo-compounds. Aqueous solutions of nitroethane, for example, are completely inert toward diazo-compounds. Such a solution of nitroethane, forming a salt and containing nitronic acid instantly after acidification of the aqueous solution, reacts with phenyldiazotate with formation of azo-compounds (or, correspondingly, phenylhydrazone) [67].



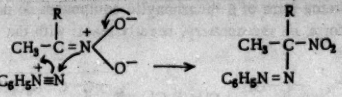
The sodium salt of nitroethane reacts with phenyldiazonium chloride with formation of the azo-compound [68]:



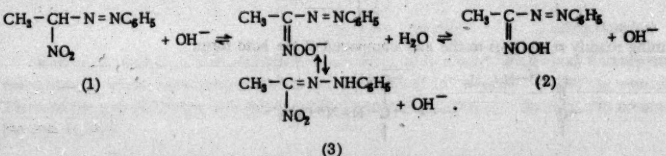
Thus, from the aryldiazonium polyhalide, the diazo-compound is formed:



The fact that the actual nitro-compound does not react with the diazo-compound, but nitronic acid or its salts do react with it, forming true azo-derived nitro-compounds (this is absolutely accurate for azo-coupling of secondary nitroparaffins or for secondary azo-coupling of the primary nitro-compounds; there is no basis for assuming that the first azo-coupling of the primary nitro-derivatives takes place in any way differently), testifies in favor of the concepts on the course of the azo-coupling reactions with transfer of reaction center:



In the case of 2-nitropropane (R = CH_3) this reaction also is accomplished. If R = H, then tautomerization occurs:



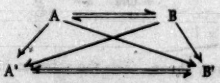
(1) (2)

(3)

The anion forming had the capacity for forming a new azo-coupling with sufficiently active diazo-components:

If the same diazo-compound is not sufficiently active, then the reaction stops at the first stage, at which the product seems to be the hydrazone (3), in the direction of which, since it is least acid, the tautomeric equilibrium is displaced.

In the field of aliphatic nitro-compounds we succeeded in observing all the possible ways of formation of the two series of derivatives according to the most complete scheme 7.



(Scheme 7)

Transition A ⇌ B is a tautomeric transformation. A → A', for example, the reduction of a nitro-compound to the amine:

$$CH_3NO_2 \rightarrow CH_3NH_2.$$

B → B' – methylated aci-form of diazomethane:

$$R-CH=NOOH + CH_2N_2 \rightarrow R-CH=NOOCH_3 + N_2.$$

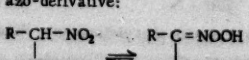
A → B' – formation of a salt from nitro-compound:

$$CH_3NO_2 + NaOH \rightleftharpoons CH_2=NOONa + H_2O.$$

B → A' – formation of the azo-derivative from an aci-form:

$$R-CH=NOOH + C_6H_5N_2OH \rightarrow R-CH(NO_2)N=NC_6H_5.$$

A' ⇌ B' – tautomeric transformation of an azo-derivative:

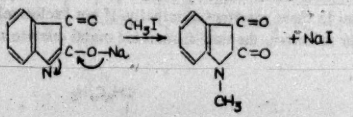


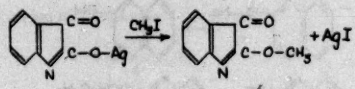
Thus, the dual reactivity of a tautomeric substance cannot be expressed merely by the simple Scheme 1. There are other possible diverse ways of forming two series of derivatives, at the basis of which lie two facts: the tautomeric equilibrium of the substances, each of which has a capacity for independent reactions, and the presence of conjugated bonds in the molecules of each of the forms, which imparts to them the capacity to react dually – with and without the transfer of the reaction center.

By which of the possible ways the formation of derivatives proceeds in each concrete case is the problem, the elucidation of which is something for the future. Occasionally we know this. Examples of such types were given above.

In many cases, judgment of this may be made only hypothetically. However, in the majority of cases, the answer to this question is still not known.

Still few are the factors that have been studied, which determine the course of a reaction with transfer of reaction center or without it. In this field we have only individual observations and partial generalizations. Thus, the relative reactivities of the salts of alkali metals, and the silver and mercury derivatives of dually reacting substances applicable to alkylation reactions by the alkyl halides, permit us to assume that, the more polar the O–Me bond, the stronger the tendency toward transfer of the reaction center to the carbon atom during the alkylation reaction. This is obvious by comparison of the alkylated silver and sodium salts of isatin and similar compounds:



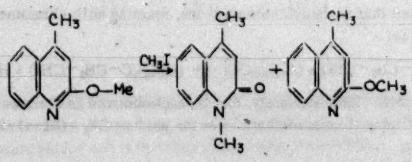


The same conclusion might be drawn from comparisons of the yields of the C- and O-methoxymethylated enolates of diphenylpropiomesitylene [69]. From the table given below it is obvious that the larger the electropositivity of the metal, the higher the yield of the C-methoxymethylated derivative:

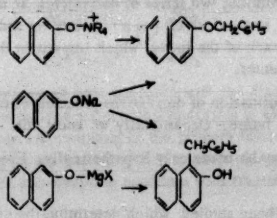
	Mg	Li	Na
C-methoxymethylated derivative	25	38	47
O-methoxymethylated derivative	75	26	8

(reaction in benzene solution)

Furthermore, according to the observations of Brady and Jakobovits [70] on the methylation of 2-hydroxylepidine by methyl iodide in a medium of methyl alcohol in the presence of the metal alcoholate

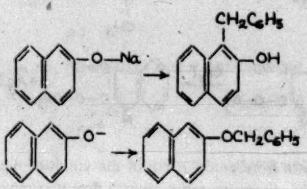


the ratio of methylated derivative $N-CH_3/O-CH_3$ increases according to the series $Na^+ < K^+ < \overset{+}{N}R_4$ in the following proportions: 4.5:10.8:∞. On the other hand, according to the observations of Nesmeyanov, Sazonova and Vasilyeva [69], the enolates of desoxybenzoin, diphenylpropiophenone and diphenylpropiomesitylene and the quaternary ammonias, benzoylate and methoxymethylate on the oxygen without transfer of the reaction center, principally before the corresponding enolates of the alkali metals and magnesium. According to the work of Nesmeyanov and Zogorevsky [71], the β-naphtholates of the quaternary ammonias also alkylate (benzyl bromide), chiefly on the oxygen. Moreover, the magnesium β-naphtholates alkylate under the same conditions, principally on the carbon, but sodium – to an equal extent, on the carbon and oxygen:

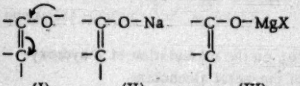


The tetramethylammonium and the sodium enolates of ethyl acetoacetate differ especially sharply in their reactions with benzoyl chloride. The tetramethylammonium derivative benzoylates only on the oxygen atom (in mixtures of ether and alcohol), and the sodium only on the carbon (in ether, and also in other solvents).

This result, at first glance unexpected, is connected with the long known facts, as an example of which we may name the benzoylation of allyl sodium phenolate, which according to Claisen, in hydrocarbon solvents, proceeds on the carbon, with transfer of the reaction center, but in alcohol – proceeds on oxygen. Both facts indicate that the enolate-anion alkylates or acylates in these reactionsprincipally, if not exclusively, on the oxygen, and for alkylation with transfer of the reaction center to carbon, the non-dissociated metal enolate molecule was necessary:



Thus, system (I) in this series of experiments had a surprisingly smaller capacity for transfer of the reaction center than (II), or especially (III), and the results of the two series of experiments are found to be in obvious contradiction. Another conclusion, which was drawn by Nesmeyanov and Zagorevsky on comparing the action of different alkylating and acylating reagents on the β-naphtholates of metals, was that the more electrophilic such a reagent, the more it tended to alkylate on the oxygen atom.



(I) (II) (III)

It has already been mentioned that triphenylchloromethane, reacting with chloromercuracetaldehyde, forms only 3,3,3-triphenylpropionaldehyde:

$$ClHg-CH_2-CHO + (C_6H_5)_3CCl \rightarrow (C_6H_5)_3C-CH_2-CHO + HgCl_2.$$

The alkylation proceeds on the carbon. Simultaneously, one product observed in the reaction of the same mercury-organic substance with tri-p-nitrotriphenylbromomethane, was the product $CH_2=CH-O-C(C_6H_4NO_2)_3$, forming with transfer of the reaction center.

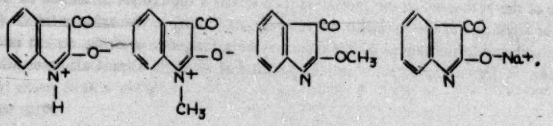
The reaction of triphenylmethane halide with sodium phenolate gave a mixture of O- and C-alkylated products, whereas tri-p-nitro-triphenylbromomethane alkylated sodium phenolate exclusively on the oxygen, without transfer of the reaction center. 2,4-Dinitrobromobenzene also alkylates β-naphthol only on oxygen. Thus, since the matter relates to the reagent attacking the metallic derivative of the keto-enol type of system, the matter sums up thus, that the more electrophilic the reagent, the more rapidly it reacts with oxygen rather than with carbon, independently of whether the reaction occurs with or without transfer of reaction center.

All of this conforms to such a picture.

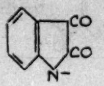
In the system outside the reaction, the charge concentrated mainly on the oxygen atom. This

follows from the similarity of the absorption spectra of the metal enolates and alkyl esters of the enols. Analogously in the system the charge (and in the nonionized metal derivative – metal) is connected with the oxygen and is not distributed to any considerable degree on the nitrogen atom. The system of bonds of the lactam , apparently, is not at all realized; instead of it, the system exists.

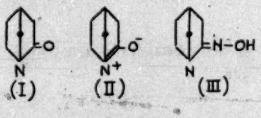
Investigation of the absorption spectra of the most important lactim-lactams, for example isatin [73], showed great similarity of the spectra and, consequently, distribution of the electronic density both for the lactim-lactams (having the lactam structure), and for their alkali salts and N- and O-derivatives. This is possible only for the following distribution of bonds and charges:



If the anion structure corresponded to the formula



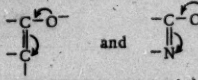
then its spectrum would differ sharply from that of the remaining form. The impossibility of the existence of the bicyclic system (I), frequently cited by Nesmeyanov and Tolstoi and also well-known earlier from the literature [72], may be used as evidence for the use of the "betaine" structure of the lactam. One naturally explains the impossibility of shifting the bond



in form (II) in connection with the impossibility of formation of multiple bonds at the head of the bicyclic bridge (Bredt Law). Moreover, the oximes of this type of bicyclic structure do exist as (III); in them, it is not possible for nitrogen to become ammoniated and it becomes structurally impossible.

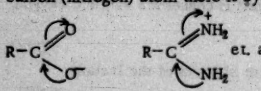
According to the discussion, it should be considered that the metallic derivatives of the lactim-lactam or keto-enols have the lactim, or accordingly, the enolate structure.*

This conclusion does not conflict with the prevailing concepts of the distribution of the ionic charge in similar systems between atoms of oxygen and nitrogen (carbon), in accordance with the scheme:



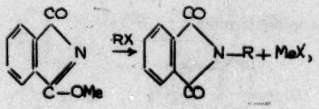
* Only the mercury derivatives of the type given above, mercurized the oxo-compounds or the like, since the mercury salt of cyanuric acid seems to be a keto (aldehydic) or lactam derivative, containing the C–Hg or N–Hg bond.

There is no basis for maintaining that a complete ionic charge is attached to the oxygen atom, and on the carbon (nitrogen) atom there is by no means an effective negative charge. On the contrary, there is much basis for assuming that the charge is distributed between the ends of the triads in accordance with the scheme given. There is a similar alignment of the charges completely in the symmetrical systems of the type in which, at the ends of the triads, are found atoms of the same element. However, in anions of the enols or lactims at the ends of the triads atoms of different elements are found, which differ essentially in their electronegativities (oxygen and nitrogen, oxygen and carbon), and the distribution of the charge may not be symmetrical, but it is concentrated chiefly on the more electronegative oxygen. At the moment of attack of the electrophilic reagent on the carbon or nitrogen, a considerable redistribution of the electronic density proceeds. The direction and rate of reaction, therefore, should be determined not so much by the magnitude of the effective charge on the carbon (nitrogen) (it must in all cases be small) as by the capacity of the conjugated system for the reactions necessary for redistribution of the electronic density.

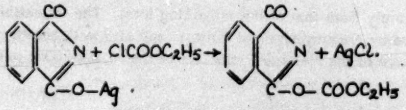


Proceeding from the salts of the keto-enols or the lactim-lactams, we determined the action of several fundamental factors, each of which contributed to a more rapid occurrence of either O- or C-reactions.

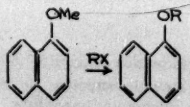
The structure of the keto-enol or the lactim-lactam exerts a substantial influence on the direction of the reactions of alkylation or acylation of the metallic derivatives. According to the affinity for C- (or, accordingly, N-), the reactions of the tautomeric substances of this type may be arranged in a series, on one end of which would be found such substances, as, for example, phthalimide, the salts of which, in almost all cases, alkylate or acylate on the N:



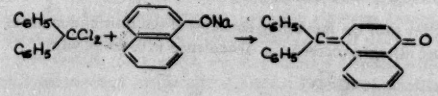
and only the silver salt (but not the sodium) forms O-acylated derivatives with ethyl chlorocarbonate [74]



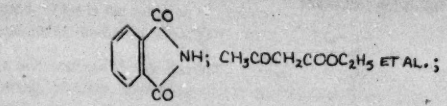
At the opposite end of this series occur such substances as α-naphthol, for which alkylation and acylation of the salts almost always proceeds on the oxygen:

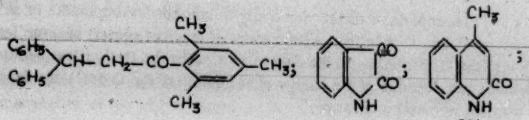


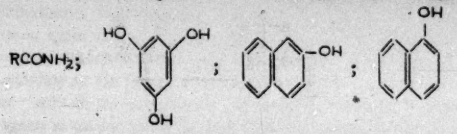
Examples of C-reactions are extremely few: the Kolbe reaction, for alkylation of sodium naphtholate by benzyl chloride, and the action of benzophenone chloride on it [75]:



The keto-enols and lactim-lactams discussed in the present report are arranged in this series approximately in the following form:







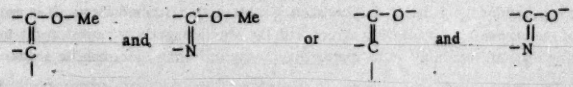
The phthalimide salts, as mentioned, have the capacity, almost exclusively, for N-reactions. Salts of ethyl acetoacetate and similar keto-enols form essentially the C-derivatives on alkylation and acylation; the O-derivatives are obtained by reaction of sodium salts with ethyl chloromethylate or ethyl chlorocarbonate, by reaction of pyridine salts with acyl chloride in a pyridine medium (Claisen reaction), and by alkylation and acylation reactions of silver or copper salts.

The alkali and magnesium salts of substances of the diphenylpropiomesitylene type are alkylated on the carbon atom by alkyl halides, but with chloromethyl ether (more electrophilic), they form both C- and O-derivatives. The same is observed also for the benzolyated salts of these. Salts of isatin and other lactim-lactams (including the acyclic acid amides) have the capacity for N- and O-alkylation, depending on the nature of the metal and the reagent; in addition to that, the sodium salts are principally alkylated on the nitrogen atom by the alkyl halides, and the silver salts are alkylated on the oxygen atom. The sodium salt of α-hydroxylepidine, however, forms about 20% of the O-derivative with methyl iodide [70].

Sodium- or potassium-phloroglucinol is alkylated chiefly on the carbon atom by methyl iodide or ethyl iodide. However, we always observed, in addition, a simultaneous O-alkylation, which under certain conditions became prominent [76].

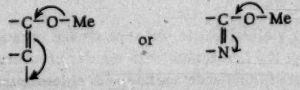
Alkylation of the salts of β-naphthol, as pointed out, depends on the metal and the reagent to a substantial extent; moreover, O-alkylation is always observed for the simple alkyl halides. For benzyl bromide or allyl chloride, under certain conditions, C-alkylation predominates [71].

Finally, as already observed, the salts of α-naphthol tend almost exclusively toward O-reactions. Thus, in the series given above, going from the first member to the last, the systems



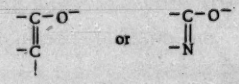
all have less tendency for reaction with transfer of the reaction center.

The next important factor determining the direction of the reaction of the salts of the keto-enols and the lactim-lactams, undoubtedly appear to be the nature of the reagent and the character of the metal-to-oxygen bond, which in turn determines the nature of the metal and the conditions of the medium. In reactions with relatively weak electrophilic reagents, such as the alkyl halides, the concept expressed at the beginning of this section was: the more electropositive the metal, the more rapidly the C-reaction (correspondingly, the N-reaction) proceeds, with transfer of the reaction center. In other words, the more "contributing" the O–Me bond appears to be

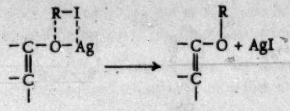


the more rapidly the reaction at the opposite end of the conjugated system of bonds proceeds. To the greatest extent, this effect is observed for the quaternary ammonium salts (in any medium), and for alkali salts in either aqueous

or alcoholic solutions, where the following ions react



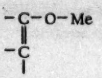
On transition to a less electropositive metal, especially in non-conducting media or in media in which the salts of these metals are not soluble, C-reactions (with transfer of reaction center) become less favored. With this, they begin to compete with the O-reactions. In the case of silver salts the O-reactions become predominant. It is possible that in such cases, the decrease of the energy of activation of the O-reactions depends also on the presence of the auxiliary reaction of metal and halide:



Silver salts of the keto-enols, lactim-lactams and acid amides are alkylated on the oxygen atom by alkyl halides. Likewise, copper salts of ethyl acetoacetate benzoylate on oxygen.

The picture changes essentially on transition to the strongly electrophilic reagents. For reactions of alkali or quaternary ammonium salts with cations or strongly electrophilic molecules, the reaction is accomplished on the oxygen atom. It proceeds, likewise, by combination of ions with a small energy of activation and, naturally, overtakes the slower reaction of C-alkylation or acylation. In a similar way, the sodium salt of ethyl acetoacetate reacts with chloromethyl ether or with chlorocarbonic ether, or the quaternary ammonium salt of desoxybenzoin reacts with chloromethyl ether. In these reactions, the more ionized the O—Me bond, the more rapidly the O-reaction is accomplished. Most important here, naturally, are the salts of the quaternary ammonium bases, and their bonds with oxygen can only be purely ionic under all conditions.

On transition to the less ionized O—Me bond, as occurs, for example, for the enolates of the alkali metals, or to a still greater degree for the enolates of magnesium in solvents having small dielectric constants, the uncharged molecule (A) reacts, eliminating the reason for the sharp decreases of the energy of activation for reactions on oxygen, and the differences of reactions on oxygen and carbon are equalized; and, all the more, the reaction on carbon may attain predominance, since nothing prevents the meeting of the attacking electrophilic molecules with carbon, and for the oxygen there is a deterrent in the form of a positive metal atom. Moreover, the pair of electrons necessary for bringing about the bond with the attacking electrophilic reagent, is easily supplied by the system of $\sigma\pi$-conjugated bonds. This effect is most obvious for salts of the heavy metals. The copper salt of ethyl acetoacetate, in contrast to the sodium salt, is acylated by ethyl chlorocarbonate on the carbon atom [77]. Likewise, this salt reacts with chloromethyl ether on the carbon atom [78].



(A)

Thus, besides the series of dually reacting substances described above, it is necessary to take into account a series of metals (which, apparently, agrees with the electronegativity series) and a series of reagents. For the alkylating reagents, one may write approximately the following electrophilic series:

$$\{RI;\ R_2SO_4;\ CH_2{=}CH{-}CH_2Cl;\ C_6H_5CH_2Br\}\quad CH_3OCH_2Cl;\ (C_6H_5)_2CCl_2;\ (C_6H_5)_3CCl;\ (NO_2C_6H_4)_3CBr.$$

For acylating reagents we may write:

$$RCOCl;\ ClCOOC_2H_5;\ RCON\overset{+}{<}\ ]\ Cl.$$

The observed mechanism may be summarized in the following way.

1. If the O—Me bond is strongly ionized, and the reagent is a cationic or strongly electrophilic molecule, then the rapid O-reaction occurs. Here belong the O-acylations, and according to Claisen, other O-reactions of ammonium salts with strongly electrophilic reagents, and the O-acylation of the sodium derivatives of ethyl acetoacetate, ethyl chlorocarbonate, etc.,

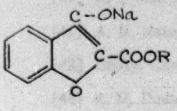
2. If the reagent is also strongly electrophilic, then the O—Me bond is not ionized, or is weakly ionized, and the O-reaction proceeds more slowly; the C-reaction, with transfer of reaction center, begins to predominate. This is how the reaction of the copper salt of ethyl acetoacetate with chloromethyl ether or ethyl chlorocarbonate proceeds.

3. The same result is observed also in the opposite case, when the reagent is not very electrophilic, but the O–Me is strongly ionized. This is the reaction of alkylation of the lactim-lactams and the keto-enols, by alkyl halides, better – in conducting media, or accordingly, in acylation (benzoylation) reactions.

4. Finally, for a non-ionized O–Me bond and a weakly electrophilic reagent, the O-reaction again takes place, at this time slowing, possibly, depending on the type of the four-membered transition complex presented above. Here, for example, belong the C- and N-alkylation by alkyl halides, of silver salts of the lactim-lactams and keto-enols.

It is necessary to bear in mind that to some extent the degree to which the reagent is electrophilic in reactions of alkylation or acylation of the salts of dually reacting substances, also depends on the nature of the latter. Thus, for alkylation or acylation of the salts of phthalimide, all the reagents are known to be weakly electrophilic. For the potassium salts of phthalimide, they enter into reaction on the nitrogen. Ethyl chlorocarbonate reacts with silver salts on the oxygen atom, again as a weakly electrophilic reagent. Toward β-naphthol, found at the opposite end of the series, all the reagents are known to be strongly electrophilic. In accordance with this, the salts of ammonia are alkylated predominately on the oxygen atom, the sodium salts – on both oxygen and carbon, and the salts of magnesium and zinc – only on the carbon atom. Moreover, O-reactions for salts of the alkali metals are also propagated by such reagents as methyl iodide or dimethylsulfate, which are known in this case to be strongly electrophilic reagents.

For the remaining substances, the transition from strongly electrophilic reagents to weak ones is accomplished at some place in the series, depending on the nature of the dually reacting substance. Thus, for the sodium derivative of ethyl acetoacetate and similar keto-enols, both the alkyl halides and dimethylsulfate react as weakly electrophilic reagents, with the formation of C-derivatives. However, in the reactions of the sodium derivatives (A) of dimethylsulfate, in contrast to methyl iodide, the oxygen is alkylated and this demonstrates its strong electrophilic nature in the present case [79]. Benzoyl chloride, with the sodium derivative of ethyl acetoacetate – a reagent still weakly electrophilic – benzoylates on the carbon atom (although trimethylammonium salt is already benzoylated on the oxygen), but for the sodium derivative of naphthol, the same benzoyl chloride is sufficiently electrophilic to acylate on the oxygen atom.



(A)

Thus, the series of substances and reagents given above form a kind of sliding scale, in which each substance is established at a definite relative position. Thus, for phthalimide, the range of reagents occupies the extreme left positions (all the reagents are weakly electrophilic). This range gradually shifts to the right with the degree of transition from phthalimide to subsequent substances in the series, and occupies the extreme right position for naphthol (all reagents are strongly electrophilic). The same also holds for the metals.

Thus, the simple and clear Scheme 1, accepted into the theory of tautomerism in the first half of our century, seems to correspond to only one of the possible ways of forming two series of derivatives. The capacity for dual reactions is a phenomenon incomparably more widespread than tautomerism. The latter seems to be only a special case of it, since the very formation of the most important and widespread forms of tautomerism is due to the capacity for dual reactions of the molecule of the tautomeric substance: the mutual transformation of tautomers, at least at one stage, proceeds with the transfer of the reaction center. Besides, very many examples are known where the dual reaction arises independently of tautomerism; it owes its formation not to tautomerism, but to the presence in the molecule of systems of atoms with conjugated bonds, and the capacities of these systems of atoms for reactions with transfer of the reaction center (according to the 1-4-type).

The most pressing problem seems to be the further thorough study of the reactivity of conjugated systems, the elucidation of factors determining the course of reactions with and without transfer of the reaction center, the effects of the structures of the reacting organic molecules, the character of the conjugated systems, the nature of the reagent, and the conditions and media of the reactions.

Regarding the reactivities of tautomeric substances, the state of our knowledge in the field is now such that we may clearly formulate what their specificity consists of, what possible routes there are for reaction, which we know reliably in this field, and what problems still are subject to elucidation. Many of these problems, which of late have seemed to be solved, were solved incorrectly, and this requires new investigations, methods for which may be proposed. In future works on studies of the reactivities of tautomeric substances, kinetic methods of investigation should play a prominent role. They will help to explain in what way, in certain concrete cases, the dual reaction arises, what the mechanism of formation of derivatives is, and what factors determine the rate of the mutual transformation and the reaction of the tautomeric forms.

LITERATURE CITED

[1] A. M. Butlerov, J. Russ. Chem. Soc., 9, 38-76 (1877); Collected Works, Acad. Sci. USSR Press, Vol. I, 322-349 (1953).

[2] C. Laar, Ber., 18, 648 (1885); 19, 730 (1886).

[3] L. Claisen, Ann., 291, 25 (1896).

[4] W. Wislicenus, Ann., 291, 147 (1896).

[5] K. H. Meyer, Ann., 398, 64-65 (1913).

[6] L. Knorr, Ann., 293, 88 (1896).

[7] P. P. Shorygin. Advanced Organic Chemistry, State Chem.-Tech. Press, M.-L., 1932, p. 71.

[8] A. E. Chichibabin, et. al., J. Russ. Phys.-Chem. Soc., 53, 193, 213 (1921); 58, 400, 406, 421 (1926); Ber., 54, 814, 822 (1921); 55, 998 (1922); 57, 2092 (1924); 58; 1704, 1708, 1712 (1925); 59, 2048, 2055 (1926); 60, 1607 (1927).

[9] L. Knorr, Ann., 306, 332 (1899).

[10] Ch. Ingold, I. F. Thorpe, Some New Aspects of Tautomerism, 1923; cited by J. Baker. Tautomerism, United-Sci.-Tech. Press, 1937, p. 11.

[11] W. Hückel, Theoretische Grundlagen der Organischen Chemie, Leipzig, 1949, p. 205 ff.

[12] L. Claisen, E. Haase, Ber., 33, 12 (1900).

[13] L. Claisen, Ann., 422, 223 (1925).

[14] A. Michael, J. prak. Chem., [2], 37, 486 (1888); 46, 189 (1892).

[15] W. Hückel, loc. cit., p. 287.

[15a] G. V. Chelintsev, Prog. Chem., 7, 5 (1938).

[15b] W. Hückel, Theoretical Fundamentals of Organic Chemistry, Russian translation, 2nd ed., United Sci.-Tech. Press, 1935, p. 211.

[16] F. Arndt, C. Martius, Ann., 499, 262, Example 1; B. Eistert, Sammlung chem. und chem.-techn. Vorträge, N. F., 40, 126, ff. (1938).

[17] J. Baker. Tautomerism. (Russian translation). United Sci.-Tech. Press, 1937.

[18] H. Henecka, Chemie der beta-Dicarbonylverbindungen, Springer Verlag, 1950, p. 33.

[19] A. N. Nesmeyanov, V. A. Sazonova, E. B. Landor, Proc. Acad. Sci. USSR, 63, 395 (1948); A. N. Nesmeyanov, V. A. Sazonova, Bull. Acad. Sci. USSR, Div. Chem. Sci., 1949, 422; A. N. Nesmeyanov, V. A. Sazonova, E. I. Vasilyeva, Bull. Acad. Sci. USSR, Div. Chem. Sci., 1952, 78.*

[20] A. N. Nesmeyanov, Sci. Rep. Moscow State Univ., 132, 5 (1950).

[21] A. N. Nesmeyanov, I. F. Lutsenko, Bull. Acad. Sci. USSR, Div. Chem. Sci., 1947, 63; Proc. Acad. Sci. USSR, 59, 707 (1948); A. N. Nesmeyanov, I. F. Lutsenko, Z. M. Tumanova, Bull. Acad. Sci. USSR, Div. Chem. Sci., 1949, 601; Sci. Rep. of the Moscow State Univ., 132, 44 (1950).

[22] E. H. Farmer, C. D. Lawrence, J. F. Thorpe, J. Chem. Soc., 1928,729.

[23] Ph. C. Stevens, J. Am. Chem. Soc., 57, 1112 (1935).

[24] E. P. Kohler, H. Baltzly, J. Am. Chem. Soc., 54, 4015 (1932); Wm. G. Joung, J. D. Roberts, J. Am. Chem. Soc., 66, 2131 (1944); 68, 1472 (1946).

[25] J. Baudrenghien, Bull. Soc. Chim., [4], 31, 681 (1922).

[26] A. N. Nesmeyanov, R. Kh. Freidlina, J. Gen. Chem., 7, 43 (1937); S. L. Varshavsky, Bull. Acad. Sci. USSR, 29, 315 (1940).

[27] A. M. Ward, J. Chem. Soc., 1927, 445.

* See Consultants Bureau Translation, page 89.

[28] J. Baker, "Hyperconjugation", Oxford (1952).

[29] A. N. Nesmeyanov, R. Kh. Freidlina, L. I. Zakharkin, Proc. Acad. Sci. USSR, 81, 199 (1951).

[30] D. L. Hill, et. al., J. Am. Chem. Soc., 74, 5599 (1952).

[31] K. Alder, H. Söll, Ann., 563, 75 (1949); A. Berlin, S. Sherlin, J. Gen. Chem., 8, 16 (1938).

[32] R. T. Arnold, R. W. Amidon, K. M. Dodson, J. Am. Chem. Soc., 72, 2871 (1950); R. T. Arnold, J. F. Dowdall, J. Am. Chem. Soc., 70, 2590 (1948); J. P. Bain, J. Am. Chem. Soc., 68, 638 (1946).

[33] O. Dermer, J. Hawkins, U. S. Patent 2524777, Chem. Abs., 45, 2497 (1951); U. S. Patent 2591239, Chem. Abs., 46, 11248 (1952); W. Cresham, W. Grigsoy, U. S. Patent 2493964, Chem. Abs., 44, 4508 (1950).

[34] A. N. Nesmeyanov, R. Kh. Freidlina, Acad. Sci. USSR, Div. Chem. Sci. Press, 1942, 14.

[35] O. Aschan, Chem. Zentr., 1918, 11, 953.

[36] A. E. Arbuzov, Selected Works, Acad. Sci. USSR Press, Moscow, 1952, pp. 463-464.

[37] A. N. Pudovik and B. A. Arbuzov, Bull. Acad. Sci. USSR, Div. Chem. Sci., No. 5, 522 (1949); J. Gen. Chem., 21, 382, 1837 (1951).*

[38] P. L. Julian, W. L. Cist, J. Am. Chem. Soc., 57, 2030 (1935).

[39] A. N. Nesmeyanov, R. Kh. Freidlina, A. K. Kochetkov, Bull. Acad. Sci. USSR, Div. Chem. Sci., 1949, 623.

[40] A. I. Shatenshtein, L. N. Vasilyeva, Proc. Acad. Sci. USSR, 95, 117(1954).

[41] A. N. Nesmeyanov, A. E. Borisov, Proc. Acad. Sci. USSR, 60, 67 (1948).

[42] Deasy, Chem. Rev., 36, 145 (1945).

[43] R. M. Dodson, W. P. Webb, J. Am. Chem. Soc., 73, 2767 (1951); F. Bell, W. H. Huntes, J. Chem. Soc., 1950, 2903.

[44] K. Auwers, F. Winternitz, Ber., 35, 468 (1902); K. Auwers, O. Keil, Ber., 35, 4211 (1902).

[45] L. Herzig, F. Wenzel, Monatsh., 27, 786 (1906); A. Spitzer, Monatsh., 11, 104, 287 (1890); 9, 1046, 1049 (1888); 10, 459 (1889).

[46] J. Meisenheimer, Ann., 323, 221 (1902); A. Hantzsch, J. Kissel, Ber., 32, 3142 (1899), and others.

[47] R. C. Fuson, M. D. Armstrong, S. B. Speck, J. Org. Chem., 7, 297 (1942); R. C. Fuson, M. D. Armstrong, W. E. Wallace, J. W. Kneisley, J. Am. Chem. Soc., 66, 681 (1944).

[48] E. P. Kohler, J. Am. Chem. Soc., 52, 4128 (1930).

[49] W. C. Brown, M. S. Kharasch, W. R. Sprowes, J. Org. Chem., 4, 442 (1939).

[50] M. I. Kabachnik, Collection, "Problems of the Mechanism of Organic Reactions," Acad. Sci. USSR Press, Kiev, 1954, p. 126.

[51] M. I. Kabachnik and T. A. Mastryukova, Bull. Acad. Sci. USSR, Div. Chem. Sci., 1953, 163.**

[52] M. I. Kabachnik, Proc. Acad. Sci. USSR, 83, 407 (1952).

[53] A. Lapworth, J. Chem. Soc., 85, 30 (1904).

[54] H. M. Dawson, J. St. Cartes, J. Chem. Soc., 1926, 2282.

[55] C. M. Schwab, Handbuch der Katalyse, p. 7, Vol. I, Wien, 1943, p. 45.

[56] M. I. Kabachnik and V. A. Gilyarov, Proc. Acad. Sci. USSR, 1954, 96, 991.

[57] Ya. L. Goldfarb, O. N. Setkina, Ya. L. Danyushsvsky, J. Gen. Chem., 18, 124, 132 (1948).

[58] Ya. L. Goldfarb, Ya. L. Danyushevsky, Proc. Acad. Sci. USSR, 79, 245 (1951); Bull Acad. Sci. USSR, Div. Chem. Sci., 1953, 154.***

* See Consultants Bureau Translation, pages 423, 2035.

** See Consultants Bureau Translation, page 145.

*** See Consultants Bureau Translation, page 137.

[59] O. Piloty, and coworkers, Ber., 31, 452 (1898); 35, 3093, 3101, 3113 (1902).

[60] W. Charlton, J. C. Farl, J. Kenner, A. A. Luciano, J. Chem. Soc., 1932, 30.

[61] J. N. Brönsted, Z. phys. Chem., A169, 32 (1934).

[62] N. A. Izmailov, J. Phys. Chem., 24, 821 (1950).

[63] M. I. Kabachnik, Proc. Acad. Sci. USSR, 83, 859 (1952).

[64] K. H. Meyer, Ber., 47, 826 (1914).

[65] M. I. Kabachnik, S. T. Ioffe, Proc. Acad. Sci. USSR, 91, 833 (1953).

[66] O. Dimroth, M. Hartmann, Ber., 40, 4460 (1907); 41, 4012 (1908).

[67] A. Hantzsch., I. A. Kissel, Ber., 32, 3145 (1898).

[68] V. Meyer, Ambrül, Ber., 8, 751, 1073 (1875); E. Bamberger, L. Frei, Ber., 36, 3833 (1903).

[69] A. N. Nesmeyanov, V. A. Sazonova, E.Vasilyeva, Bull. Acad. Sci. USSR, Div. Chem. Sci., 1952, 85;* Proc. Acad. Sci. USSR, 63, 398, (1948).

[70] O. L. Brady, J. Jakobovits, J. Chem. Soc., 1950, 767.

[71] V. A. Zagorevsky, Dissertation, Moscow State Univ. (1954).

[72] N. L. Leonard, C. Z. Schoemaker, J. Am. Chem. Soc., 71, 1876 (1949); F. S. Fancett, Chem. Rev., 47, 219 (1950); L. Lukas, Coll. of Czechslov. Chem. Commun., 10, 148 (1938).

[73] P. C. Ault, E. L. Hirst, R. A. Morton, J. Chem. Soc., 1935, 1653.

[74] C. Heller, P. Jacobsohn, Ber., 54B, 1107 (1921).

[75] C. W. Clough, J. Chem. Soc., 89, 773 (1906).

[76] J. Herzig, F. Wenzel, Monatsh., 27, 785 (1906).

[77] E. Näf, Ann., 266, 110 (1891).

[78] I. L. Simonsen, R. Storey, J. Chem. Soc., 95, 2108 (1909).

[79] K. Auwers, Ber., 45, 994 (1912).

Received July 3, 1954

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* See Consultants Bureau Translation, page 87.

STRUCTURAL DIRECTABILITY OF THE DIENE SYNTHESIS

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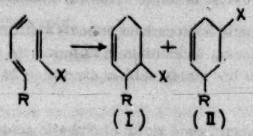
The structural directability of the diene synthesis with the participation of asymmetric dienes and dienophiles has been insufficiently treated in the literature. Isolated, fragmental data make it impossible to build up a complete picture of the formation of the structural isomers.

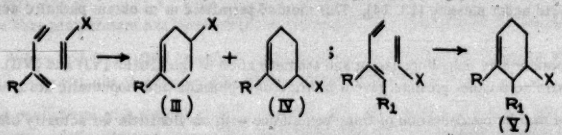
The purpose of the present work was a systematic investigation of the directability of the diene synthesis of asymmetrically substituted dienes with different asymmetric dienophiles.

Careful setting up of the experiments of fractional distillation of the reaction products with an efficient column and development of methods of dehydrogenation and oxidation giving high yields permitted us to analyze the intricate picture of the products forming. The diene condensation reaction of asymmetrically substituted dienes with asymmetric dienophiles may proceed in two directions. For the dienes substituted in position 1, the formation of addition compounds having ortho- and meta-orientations is possible:



(I) (II)

Dienes, substituted in position 2, may form addition compounds having para- and meta-orientations:



(III) (IV) (V)

On the basis of the work of Alder [1] and other investigators [2, 3], it has been considered up to now that the dienes substituted in position 1 (the pentadiene type), on condensation with an asymmetric dienophile yield only addition compounds of the ortho-orientation (I). Actually, Frank, Emmick and Johnson [4] by condensation of pentadiene with acrylonitrile succeeded in demonstrating the presence of about 15% of the meta-isomer (II) in the reaction products. However, this conclusion has not found confirmation in the latest works of other investigators [5, 6, 7].* Much literature data on the condensation of asymmetric dienophiles with the dienes substituted in position 2 (isoprene type), indicates, that the chief product in these condensations is the para-isomer (III). Careful investigations of the addition products in certain cases have recently [8, 9, 10] established the presence in the latter of from 2 to 30% of the meta-isomer (IV).

For dienes substituted in the 1,2 position, in the majority of cases only addition compounds having the ortho-orientation (V) were isolated, which was shown by an example of cyclic dienes of vinylcyclohexene and vinyloctaline in the report from our laboratories [11, 12].

For careful investigation of the structural directability of the diene synthesis, we chose trans-pentadiene, isoprene, 2-tert-butylbutadiene, 1,2-dimethylbutadiene and 1-vinyl-Δ^1-cyclohexene as the asymmetric dienes.

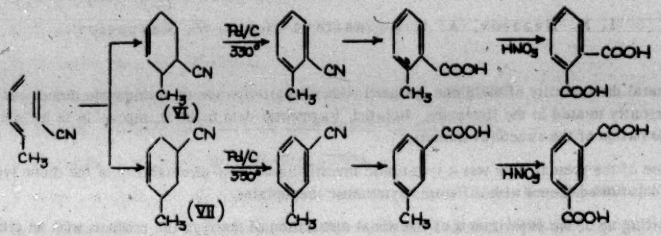
The methyl ester of acrylic acid, the methyl ester of metacrylic acid, acrylonitrile, trans-crotonic acid, and styrene were used as the asymmetric dienophiles.

As an example, the condensation of pentadiene with acrylic ester and styrene showed that the use of iodine as an inhibitor increases the yield of addition compounds by more than twice. This fact is connected with the isomerizing

* Only recently, after the completion of our work, Alder [7] succeeded in observing the meta-isomer in the condensation products of 1-tert-butylbutadiene with acrylic acid.

action of iodine; therefore, for the subsequent diene condensation, pentadiene isomerized beforehand with iodine and containing 92% of trans-pentadiene was used.

By heating trans-pentadiene with acrylonitrile for a period of 12 hours at 100°, a mixture of cyclic nitriles (VI) and (VII) in a 10:1 proportion was obtained in 30% yield.



Upon dehydrogenation of a mixture of nitriles (VI) and (VII) by palladium on carbon, and saponification of the dehydrogenation product, a mixture of toluic acids was obtained, and from it we succeeded in isolating, by crystallization, only one of the acids in pure form, the o-toluic acid. Because of the close solubilities of o- and m-toluic acids and the small quantity of m-toluic acid in the mixture, we were not successful in isolating the m-toluic acid in the pure form; therefore, the mixture of toluic acids was oxidized further to the phthalic acids.

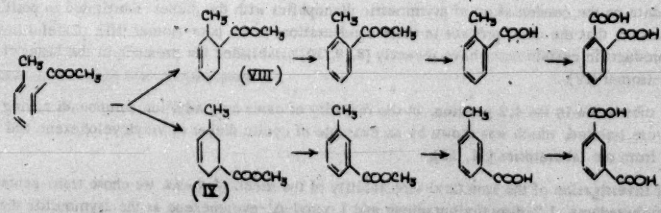
Oxidation of the ortho-substituted aromatic hydrocarbons presents a difficult problem. Such oxidizing agents as chromic anhydride in acetic acid and potassium dichromate in sulfuric acid decompose the hydrocarbon. Oxidation by permanganate or 30% nitric acid gives low yields, seldom exceeding 20-25%, during which together with phthalic acids, toluic acids also form.

After several unsuccessful attempts to obtain good yields of phthalic acids, using old methods (permanganate, chromic anhydride, boiling with nitric acid), we turned our attention to oxidation of the ortho-substituted hydrocarbons with dilute nitric acid under pressure [13, 14]. This method permitted us to obtain phthalic acid in a high yield (80-90%).*

The toluic acids obtained by dehydrogenation and saponification of the nitriles (VI) and (VII), as a result of oxidization by dilute nitric acid under pressure gave a mixture of o-phthalic and isophthalic acids in a 10:1 ratio.

Thus, it was shown that by condensation of trans-pentadiene with acrylonitrile we actually obtained a mixture of ortho- and meta-isomers (VI) and (VII), which were observed for the first time by Frank, Emmick and Johnson [4].

By heating an equimolecular mixture of trans-pentadiene with methylacrylate for a period of 2 hours at a temperature of 230°, we also obtained, in a total yield of 82%, the isomeric addition compounds (VIII) and (IX) in an approximately 6:1 ratio.

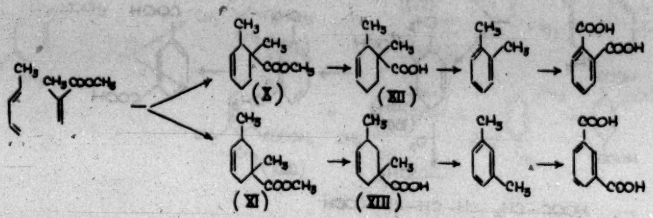


By dehydrogenation of a mixture of addition compounds (VIII) and (IX) by palladium on carbon, and saponification of the esters to obtain a mixture of toluic acids, we succeeded in isolating in the pure form only o-toluic acid; therefore, the mixture of acids was further oxidized by permanganate, in the same way as with the dilute nitric acid under pressure. Moreover, in both cases, o-phthalic and isophthalic acids were isolated in a 6:1 ratio.

* After completion of our work, a report by Bengtsson [15] appeared, which dealt with the oxidation of the xylenes and cymene under these conditions. His results agree with ours.

Thus, it was found that the diene condensation of pentadiene with methylacrylate also leads to formation of a mixture of isomeric addition compounds (VIII) and (IX), with a sharp predominance of the ortho-isomer (VIII), which, according to literature data [5], is considered to be a natural product of this condensation.

Condensation of trans-pentadiene with the methyl ester of metacrylic acid at 200° for a period of 2 hours gave a mixture of the addition compounds (X) and (XI) in a yield of 55% with sharp predominance of the ortho-isomer (X):



By saponification of the addition compounds (X) and (XI), a mixture of the liquid acids (XII) and (XIII) was obtained, which on dehydrogenation by palladium on carbon, formed a mixture of xylenes. Oxidizing the xylenes with dilute nitric acid under pressure, we obtained a mixture of o-phthalic and isophthalic acids in a 14:1 ratio. By oxidation of these xylenes with a solution of permanganate or by boiling with 30% nitric acid, we succeeded in obtaining only a small quantity of o-toluic acid.

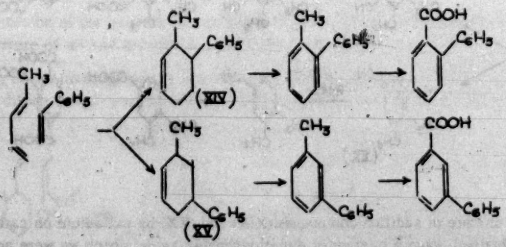
Condensation of trans-pentadiene with the methyl ester of metacrylic acid was carried out also at 100°, for the purpose of determining whether the reaction temperature affects the ortho- and meta-isomer contents.

After saponification of the addition compounds (X) and (XI), obtained at 100°, the mixture of acids (XII) and (XIII) was dehydrogenated, and oxidation of the mixture of xylenes with dilute nitric acid under pressure gave o-phthalic and isophthalic acids in a 12:1 ratio.

This shows that temperature has little effect on the proportion of isomers in the reaction product.

Recently, Petrov and Sopov [16] described condensations of pentadiene and isoprene with the methyl ester of methacrylic acid; however, the structure of the product obtained was not proved.

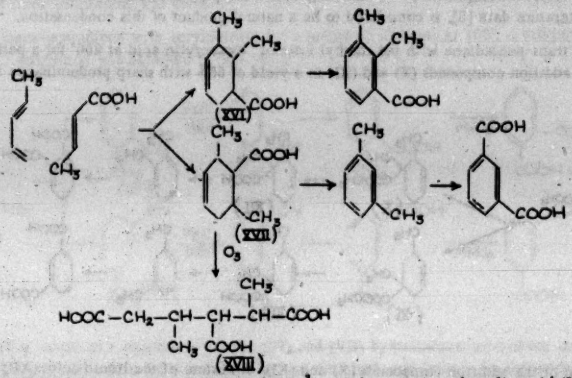
By heating pentadiene with styrene at approximately 200° for a period of 2 hours, we obtained in yields of about 40%, a mixture of the addition compounds (XIV) and (XV), with sharp predominance of the ortho-isomer (XIV):



By dehydrogenation of the addition compounds (XIV) and (XV) by palladium on carbon, and oxidation of the dehydrogenation products by permanganate, we obtained, together with o-phenylbenzoic acid, about 15% of m-phenylbenzoic acid.

Attempts to distil the addition compounds from pentadiene and acrylonitrile, and from the methyl ester of metacrylic acid and styrene, in a column of 50 theoretical plates, were not successful.

Upon condensing trans-pentadiene with trans-crotonic acid at 240° for a period of 2 hours we obtained, in a total yield of about 50%, a mixture of the crystalline and liquid addition compounds (XVII) and (XVI) in approximately a 10:1 ratio.



Dehydrogenation of the crystalline 2,6-dimethyl-Δ^3-cyclohexene-1-carboxylic acid (XVII) by palladium on carbon or sulfur did not give the expected 2,6-dimethylbenzoic acid, but only the product of decarboxylation (m-xylene), which was oxidized by permanganate to isophthalic acid.

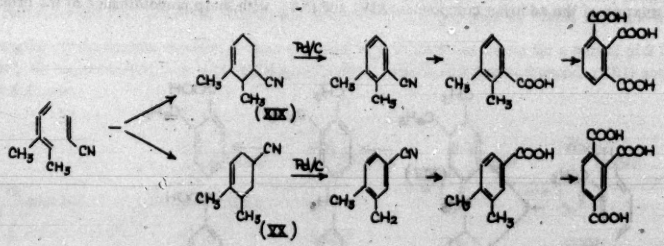
By ozonization of the crystalline acid (XVII), we obtained 1,3-dimethyl-2-carboxyadipic acid (XVIII).

By dehydrogenation of the liquid portion of the addition compound we obtained a small quantity of 2,3-dimethylbenzoic acid (total yield about 10%), which could be formed in this experiment only from the acid (XVI).

Thus, condensation of pentadiene with the asymmetric dienophiles led in all cases to the formation of a mixture of addition compounds, 85-95% of which was the ortho-isomer, and 5-15% of which was the meta-isomer.

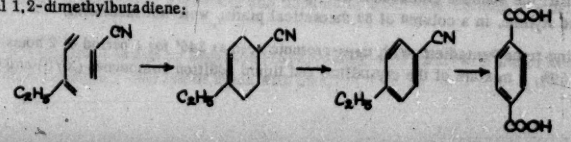
The data available in the literature [1, 2, 3] on this, for condensates that form only the ortho-isomer, require verification and corrections.

By condensation of 1,2-dimethylbutadiene with acrylonitrile at 210° for a period of 2 hours, we obtained a mixture of the addition compounds (XIX) and (XX) with a total yield of about 70%:

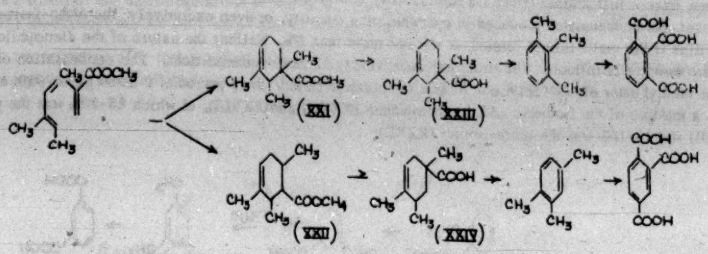


Dehydrogenation of the mixture of addition compounds (XIX) and (XX) by palladium on carbon, and saponification of the aromatic nitriles obtained, gave a mixture of dimethylbenzoic acids, which we were not able to separate by crystallization; therefore, the mixture of dimethylbenzoic acids was then oxidized by dilute nitric acid under pressure, and the benzenetricarboxylic acid was separated by crystallization. Moreover, we isolated hemimellitic, trimellitic and terephthalic acids in a 20:2:1 ratio.

Terephthalic acid was obtained, apparently, due to the small amount of 2-ethylbutadiene (about 5%) contaminating the original 1,2-dimethylbutadiene:



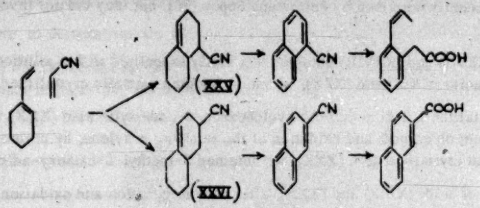
Condensation of 1,2-dimethylbutadiene with the methyl ester of metacrylic acid at a temperature of 220° for a period of two hours also gave a mixture of the addition compounds (XXI) and (XXII), in a total yield of about 50%.



As a result of saponifying the addition compounds (XXI) and XXII), a mixture of the liquid acids (XXIII) and (XXIV) was obtained. Dehydrogenation of these acids by palladium on carbon, and oxidation of the dehydrogenation product by dilute nitric acid under pressure, gave a mixture of hemimellitic, trimellitic and tetephthalic acids in a 20:3:1 ratio.

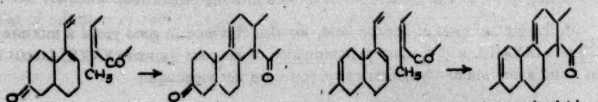
Consequently, the diene condensation of asymmetric dienophiles with 1,2-dimethylbutadiene have a structural directability, analogous to that of pentadiene; moreover, about 90% of the common ortho-isomer and only 10% of the uncommon meta-isomer were formed.

By condensation of vinylcyclohexene with acrylonitrile at 230° for a period of two hours, we obtained a mixture of bicyclic nitriles (XXV) and (XXVI), in a total yield above 90%:

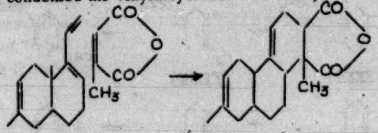


Dehydrogenation of the mixture of nitriles (XXV) and (XXVI), and saponification of the dehydrogenation products gave a mixture of α- and β-naphthoic acids in a 18:1 ratio.

A previous broad investigation in our laboratory showed that upon the diene condensation of different vinylbicyclenes with different α,β-unsaturated cyclic ketones, the ortho-isomer or the so-called "inverted" steroid ketones [17] formed:

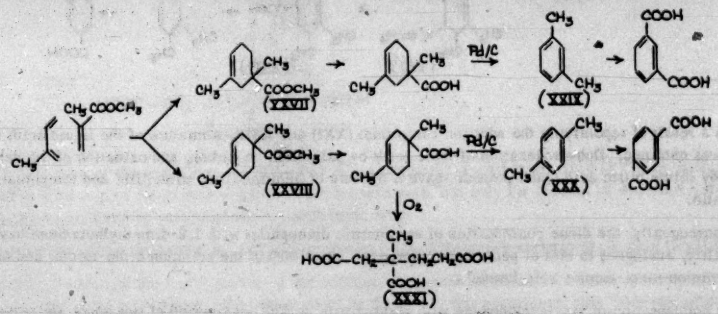


In a similar way, we condensed the vinylbicyclenes with methylmaleic anhydride:



No other structural isomers (meta-isomers) in all these condensations were found, and if they were present, they would not be present in large percentages.

Thus, the diene condensations of asymmetric dienophiles with the vinylcyclenes, and especially with the vinylbicyclenes, have a still sharper structural directability than is the case with pentadiene and 1,2-dimethylbutadiene. Moreover, the condensation produced in overwhelming quantity, or even exclusively, the ortho-isomer, and from time to time if the meta-isomer formed, it was not more than 5%. Neither the nature of the dienophile nor the temperature essentially influence the structural directability of these condensations. The condensation of isoprene with the methyl ester of metacrylic acid at a temperature of 220° for a period of 2 hours gave, with a yield of about 70%, a mixture of the isomeric addition compounds (XXVII) and (XXVIII), of which 85-90% was the para-isomer (XXVIII) and 10-15% was the meta-isomer (XXVII):



This condensation was recently described by Petrov and Sopov [16], but they did not investigate the structures of the products formed.

The mixture of esters (XXVII) and (XXVIII) obtained was easily saponified with a solution of alkali, with the formation of a mixture of the acids (XXIX) and (XXX), which on standing partially crystallized.

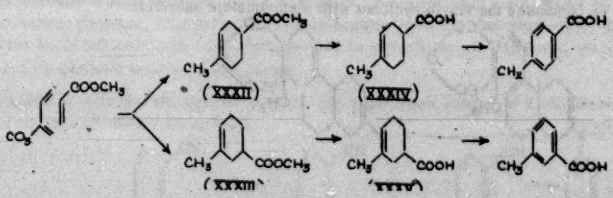
The structure of the crystalline 1,4-dimethyl-Δ^1-cyclohexene-4-carboxylic acid (XXX) was demonstrated by its dehydrogenation by palladium on carbon, and oxidation of the resulting p-xylene, by chromic anhydride, to terephthalic acid. By ozonizing the crystalline acid (XXX), we obtained 2-methyl-2-carboxy-adipic acid (XXXI).

From the liquid mixture of acids (XXIX) and (XXX), after dehydrogenation and oxidation, we obtained terephthalic and isophthalic acids, which were separated as their barium salts [18].

From the liquid mixture of acids (XXIX) and (XXX), we also obtained their corresponding amides and separated them by fractional crystallization. As a result of the saponification of the amides, the liquid acid (XXIX) was separated in the pure form, and its structure was demonstrated by its dehydrogenation and oxidation to isophthalic acid. The acids (XXX) and (XXIX) formed in an 8:1 ratio.

Condensation of isoprene with the methyl ester of acrylic acid was described by Alder [1], who found that, also, an addition product consisting of para- and meta-isomers formed in a 5:1 proportion.

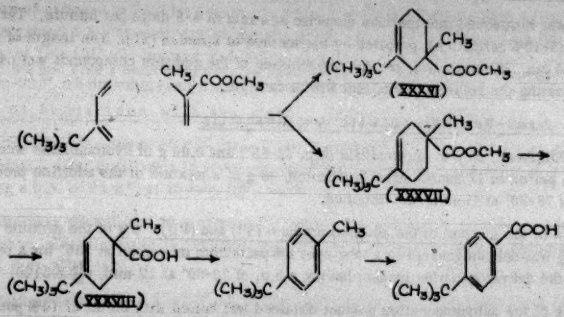
By heating isoprene with the methyl ester of acrylic acid, we also obtained in good yield a mixture of the addition compounds (XXXII) and (XXXIII), with a sharp predominance of the para-isomer (XXXII) (about 90%). Attempts to distil the esters using a column of 40 theoretical plates were not successful:



By saponification of a mixture of the esters (XXXII) and (XXXIII), a mixture of the crystalline and liquid acids (XXXIV) and (XXXV) was formed. From crystalline 1-methyl-Δ^1-cyclohexene-4-carboxylic acid (XXXIV), on dehydrogenation by palladium on carbon in a solution of benzene, p-toluic acid was obtained.

As a result of the dehydrogenation of the mixture of esters (XXXII) and (XXXIII) by palladium on carbon, and subsequent saponification, we isolated p- and m-toluic acids in a 9:1 ratio.

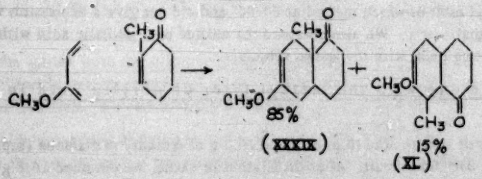
By condensation of 2-tert-butylbutadiene with the methyl ester of metacrylic acid, we synthesized the addition compounds, represented apparently, by the mixture of esters (XXXVI) and (XXXVII):



However, as a result of the saponification of this mixture, we obtained only crystalline 1-tert-butyl-4-methyl-Δ^1-cyclohexene-5-carboxylic acid (XXXVIII), the structure of which was demonstrated by its dehydrogenation to p-tert-butyltoluene, and oxidation of the latter by permanganate to p-tert-butylbenzoic acid.

We were not able to demonstrate the presence of the meta-isomer (XXXVI) in the reaction products.

As was shown in our laboratory earlier [20], by condensation of 2-methoxybutadiene with 1-methyl-Δ^1-cyclohexen-6-one, a mixture of para- and meta-isomers (XXXIX) and (XL) formed in a 85:15 ratio.



Thus, the condensation of the 2-substituted dienes (isoprene type) with asymmetric dienophiles also leads to the formation of mixtures of addition compounds, containing 80-90% of the para-isomer and 10-20% of the meta-isomer.

EXPERIMENTAL*

So-called ordinary pentadiene (b.p. 42-43°; n_D^{20} 1.4320) was separated from the distilled pentadiene fraction, obtained by the process of synthesis of divinyl, by the method of S. V. Lebedev. This pentadiene contained about 30% of the cis-form and about 70% of the trans-form. Trans-pentadiene was obtained by the isomerization of ordinary pentadiene by heating it with iodine [4], and it had the constants: b.p. 41.5°; n_D^{20} 1.4308 (content of trans-form 92%).

* Condensation of trans-pentadiene with styrene and 2-tert-butylbutadiene with methyl methacrylate was carried out by graduate-student M. V. Mavrov, of the Lomonosov Institute of Fine Chemical Technology.

1,2-Dimethylbutadiene (b.p. 76-78°, n_D^{20} 1.4460) was obtained by condensation of methyl ethyl ketone with acetylene, then partial hydrogenation of the acetylene alcohol formed, using a Pd-catalyst, producing methylethylvinylcarbinol, and dehydration of the latter over magnesium sulfate at 330°.

2-Tert-butylbutadiene (b.p. 103-105°, n_D^{25} 1.4308) was obtained by condensation of acetylene with pinacolin [19], partial hydrogenation of the acetylenic alcohol, and dehydration of methyl-tert-butylvinylcarbinol over magnesium sulfate at 330°.

The catalytic dehydrogenation of the addition products was carried out in a glass tube, of 8-9 mm diameter, heated by a vertically placed electric furnace.

The substance was introduced into the tube dropwise at a rate of 4-5 drops per minute. The catalyst was palladium on carbon (5-10% palladium), prepared by the method of Linstead [21]. The length of the layer of catalyst in the tube was 20 cm. In some cases, the dehydrogenation of the addition compounds was carried out in ampoules or by simply heating the addition compounds with a catalyst.

Condensation of trans-Pentadiene with Acrylonitrile

68 g of trans-pentadiene, 50 g of acrylonitrile (b.p. 62-63°) and 0.05 g of hydroquinone were heated in an ampoule at 100° for a period of 12 hours. After distillation, 36 g of a mixture of the addition products (VI) and (VII), having a b.p. of 78-80° at 12 mm, was obtained.

Dehydrogenation of the mixture of the addition products (VI) and (VII). 6 g of the mixture of the addition products (VI) and (VII) was dehydrogenated in a tube over 8% palladium on carbon at 330° for a period of two hours. We obtained 4.5 g of the dehydrogenation product having a b.p. of 70-80° at 12 mm, n_D^{20} 1.5120.

A mixture of 4 g of the dehydrogenation product obtained was boiled with 50 ml of 10% potassium hydroxide solution for 12 hours. The reaction product was acidified with concentrated hydrochloric acid, and the acid that formed was filtered off and dried (3.2 g).

After recrystallization from 50% methanol, o-toluic acid with m.p. of 101-102° was obtained, and the sample produced no depression of the melting point when mixed with the known substance; we did not succeed in isolating m-toluic acid.

The mother concentrate was dried, and the residue was combined with the recrystallized o-toluic acid. We obtained a total of 3.15 g of a mixture of acids, which was oxidized with 60 ml of 20% nitric acid at 170-200° under a nitrogen pressure of 30 atm for a period of 3 hours. We obtained 3.1 g of a mixture of phthalic acids, from which we recrystallized 2.7 g of o-phthalic acid from hot water; it had a m.p. of 190-191°, and gave no depression of the melting point when mixed with the known substance. Moreover, we obtained 0.28 g of isophthalic acid having a m.p. of 332-335°, the dimethyl ester of which melted at 64-65° and did not give a depression with a known sample of the dimethyl ester of isophthalic acid. We also obtained the anilide of o-phthalic acid with m.p. of 208°, which gave no depression of the melting point with the known substance.

Condensation of Pentadiene with the Methyl Ester of Acrylic Acid in the Absence of Iodine

13 g of the methyl ester of acrylic acid (b.p. 80°) and 10.3 g of ordinary pentadiene (b.p. 42°, n_D^{20} 1.4320) were heated in an ampoule at 230° for 2 hours. After distillation in vacuo, we obtained 10.5 g (45%) of a mixture of the addition compounds (VIII) and (IX) having a b.p. of 65-68° at 5 mm, n_D^{20} 1.4605.

Condensation of Pentadiene with the Methyl Ester of Acrylic Acid in the Presence of Iodine

86 g of methyl acrylate (b.p. 80°) and 68 g of ordinary pentadiene were heated with crystalline iodine in an ampoule at 230° for 2 hours. After distillation in vacuo we obtained 125 g (82%) of a mixture of addition compounds (VIII) and (IX) having a b.p. of 69-70° at 6 mm, n_D^{20} 1.4588.

Dehydrogenation and oxidation of the addition compounds (VIII) and (IX). 24 g of a mixture of the addition products (VIII) and (IX) was dehydrogenated for 20 hours at 320-330° over 5% palladium on carbon. We obtained 14 g of the dehydrogenated product (b.p. 90-107° at 40 mm, n_D^{20} 1.5100), which later was saponified by boiling with 150 ml of 10% sodium hydroxide solution for 6 hours. The reaction product was acidified, and it liberated an oil which was extracted with ether; the ether extract was dried over magnesium sulfate, and the ether was removed. The oil was allowed to stand, and 7.5 g of it partially crystallized. We obtained 3.1 g of o-toluic acid, having m.p. of 102-103°, and not giving a depression of the melting point when mixed with the known substance. Moreover, we obtained 4 g of a liquid mixture of toluic acids, from which m-toluic acid did not separate.

Oxidation of the mixture of toluic acids. 1) To 2.8 g of the liquid mixture of toluic acids described above, we added, with stirring, 1 liter of a 3% solution of permanganate at 90-95° for a period of 6 hours.

The excess permanganate was reduced by methanol, causing manganese dioxide to separate; it was removed, and the filtrate was concentrated to 150 ml. After acidification by hydrochloric acid, the solution was extracted three times with ethyl acetate. The ethyl acetate was removed, and we obtained 0.6 g of isophthalic acid having a m.p. of 332-335° (from hot water). Its dimethyl ester melted at 64-65° and did not give a depression with the known substance.

2) 2 g of the liquid mixture of toluic acids described above was oxidized by 50 ml of 20% nitric acid under a pressure of 30 atm of nitrogen at 200° for 3 hours. A solution of the reaction products was concentrated in vacuo until dry, and we obtained 1.5 g of a mixture of phthalic acids. On recrystallization from hot water, 1 g of o-phthalic acid having a m.p. of 190-191° was isolated, and did not give a depression with the known substance. Its anilide had m.p. 208° and also did not give a depression with the known substance. Moreover, we obtained 0.4 g of isophthalic acid having a m.p. of 330-335°, the dimethyl ester of which melted at 64° and did not give a depression with the known substance.

Condensation of Pentadiene with the Methyl Ester of Metacrylic Acid at 200°

1) 57 g of ordinary pentadiene, 85 g of methyl metacrylate (b.p. 100°) and 0.1 g of pyrogallol were heated at 200° for three hours. After distillation in vacuo, we obtained 28 g (20%) of a mixture of condensation products (X) and (XI) having a b.p. of 85-87° at 15 mm, n_D^{20} 1.4625.

2) 68 g of ordinary pentadiene, 92 g of methyl metacrylate and iodine crystals were heated in an ampoule at 200° for three hours. Distillation in vacuo gave 76 g (48%) of a mixture of addition products (X) and (XI) having a b.p. of 80° at 11 mm, n_D^{20} 1.4625.

3) 33 g of trans-pentadiene (b.p. 41.5°, n_D^{20} 1.4308), 50 g of methyl metacrylate and 0.1 g of hydroquinone were heated in an ampoule at 200° for two hours. We obtained on distillation 43 g (52%) of a mixture of the addition products (X) and (XI) with a b.p. of 79.5° at 10 mm, n_D^{20} 1.4620.

Found %: C 71.35, 71.36; H 9.45, 9.47. $C_{10}H_{18}O_2$. Calculated %: C 71.50; H 9.53.

Saponification of the mixture of addition products (X) and (XI). 5 g of the substance and 30 ml of 20% solution of sodium hydroxide were refluxed for 3.5 hours. The product was extracted with ether, the water-alcohol layer was acidified with 14 ml of concentrated hydrochloric acid, and the oil that separated was extracted with ether. The ether extract was dried over magnesium sulfate, the ether was removed, and the residue was distilled in vacuo. We obtained 2.5 g of a mixture of the acids (XII) and (XIII) at a b.p. of 136° at 8 mm, n_D^{20} 1.4775.

No crystals separated from the liquid acid.

Found %: C 70.26, 70.46; H 9.06, 9.03; M 150, 148.5 (titration). $C_9H_{14}O_2$. Calculated %: C 70.20; H 9.10; M 154.

Production of the amide from the liquid mixture of acids (XII) and (XIII). 5.5 g of acid (b.p. 136° at 8 mm) and 5 ml of thionyl chloride were heated at 45° for four hours. The excess thionyl chloride was removed in vacuo, and the residuals were distilled. We obtained 5 g of the acid chloride having a b.p. of 82-83° at 10 mm.

This acid chloride was added dropwise to ice for cooling, and mixed with 15 ml of concentrated ammonia solution. The amide that separated was recrystallized from hot water. We obtained 1.5 g of the amide of the acid (XII) having a m.p. of 113-114°.

Found %: N 9.27, 9.30. $C_9H_{15}ON$. Calculated %: N 9.15.

Dehydrogenation and oxidation of the mixture of acids (XII) and (XIII). 12.0 g of the liquid mixture of acids (XII) and (XIII) (b.p. 136 at 8 mm) was passed over 5% palladium on carbon at 300° for 3 hours. We obtained 7.0 g of a mixture of o- and m-xylenes having a b.p. of 130-135°, n_D^{20} 1.5047.

The isomeric composition of these xylenes was established by oxidation reactions, as described below.

1) 3.4 g of the xylene mixture (b.p. 130-135°) was boiled with 24 ml of 35% nitric acid solution for 30 hours. We obtained 0.7 g of o-toluic acid having a m.p. of 104-105°, and not giving a depression with the known substance. We did not succeed in isolating m-toluic acid.

2) 3.4 g of the xylene mixture described above was oxidized by 50 ml of 30% nitric acid solution under a nitrogen pressure of 40 atm at 200° for two hours. After recrystallization from water, 2.1 g of o-phthalic acid having m.p. of 190-191° was obtained, and it gave no depression of the m.p. with the known substance. Moreover, 0.2 g of isophthalic acid having a m.p. of 330-355° was obtained, and its dimethyl ester melted at 64-65°, and it also gave no depression of the m.p. when mixed with a sample of the known dimethyl ester of isophthalic acid. The

anilide of o-phthalic acid having a m.p. of 208° was obtained, and it gave no depression of the melting point with the known substance.

Condensation of trans-Pentadiene with Methyl Metacrylate at 100°

55 g of trans-pentadiene, 55 g of methyl metacrylate and 0.01 g of hydroquinone were heated in an ampoule at 100° for 24 hours. After distillation in vacuo, together with the initial products, we obtained 12.5 g of a mixture of the addition products (X) and (XI) having a b.p. of 118-120° at 50 mm, n_D^{20} 1.4630.

For saponification, the substance obtained was boiled with a 25% solution of potassium hydroxide for 20 hours. The reaction product was acidified with 30 ml of concentrated hydrochloric acid, and the oil which separated was extracted with ether. The ether extract was dried over magnesium sulfate. We obtained 7 g of a mixture of acids (XII) and (XIII) (b.p. 141-142° at 12 mm, n_D^{20} 1.4795), which were later dehydrogenated over 5% palladium on carbon at 305° for two hours. We obtained 3.4 g of a mixture of xylenes having a b.p. of 128-134°, n_D^{20} 1.5025.

This mixture of xylenes (3.4 g) was oxidized by 65 ml of a 25% solution of nitric acid and under 30 atm of nitrogen pressure at 200° for 4 hours. We obtained 2.8 g of a mixture of phthalic acids, from which, after recrystallization from hot water, 2.5 g of phthalic acids having a m.p. of 190-191° separated, and did not give a m.p. depression with the known substance, and 0.2 g of isophthalic acid having a m.p. of 328-330° was obtained; its dimethyl ester melted at 64.5°, and gave no m.p. depression with the known substance.

Thus, the condensation of pentadiene with metacrylate ester at 100 and 200° leads to the formation of a homogeneous mixture of addition products (X) and (XI) in a proportion of approximately 14:1.

Condensation of Pentadiene with Styrene

1) 10.5 g of ordinary pentadiene (b.p. 42°, n_D^{20} 1.4315), 15.3 g of styrene (b.p. 145.6°) and 0.1 g of hydroquinone were heated at 200° for 2 hours. A tough polymer, from which no individual products were removed, was obtained.

2) 10 g of styrene, 10 g of ordinary pentadiene and a crystal of iodine were heated in an ampoule at 200° for 2 hours. By distillation in vacuo we obtained 8.3 g (45%) of a mixture of the addition products (XIV) and (XV) having a b.p. of 106-109° at 6 mm, n_D^{20} 1.5440.

Found %: C 90.77, 90.80; H 9.44, 9.53. $C_{12}H_{14}$. Calculated %: C 90.64; H 9.36.

3) 8.2 g of trans-pentadiene, 10 g of styrene and 0.01 g of hydroquinone were heated in an ampoule at 200° for two hours. After distillation, in vacuo, we obtained 8 g (41%) of a mixture of the addition products (XIV) and (XV) having a b.p. of 114-116° at 12 mm, n_D^{20} 1.5420.

Dehydrogenation of the addition products (XIV) and (XV), and subsequent oxidation to phenylbenzoic acid. 6.5 g of a mixture of addition products (XIV) and (XV) was heated with 0.2 g of 5% palladium on carbon at 300° for 5 hours. We obtained 5.8 g of dehydrogenation products having a b.p. of 80° at 0.5 mm, n_D^{20} 1.5622.

2.9 g of the products obtained were boiled with a solution of 6 g of permanganate in 350 ml of water for 18 hours. The excess permanganate was decolorized by methanol, the precipitate of manganese dioxide was separated, and the filtrate was concentrated to $\frac{1}{3}$ of its original volume. After acidification with concentrated hydrochloric acid, o-phenylbenzoic acid (0.6 g) precipitated, and it melted at 111-112° (from aqueous methanol), and gave no depression of the m.p. with the known substance. Moreover, we obtained 0.1 g of m-phenylbenzoic acid, which after a number of recrystallizations from aqueous methanol, melted at 165.3-165.9°, and it also gave no depression of the melting point with a sample known to be m-phenylbenzoic acid.

Condensation of trans-Crotonic Acid with trans-Pentadiene

20 g of trans-crotonic acid (m.p. 71°), 26 g of trans-pentadiene and 0.01 g of hydroquinone were heated in an ampoule at 240° for 2 hours. We obtained 16.5 g of a mixture of acids (XVI) and (XVII) having a b.p. of 122-124° at 6 mm, which crystallized immediately. The crystals were pressed under a water-jet pump and recrystallized from petroleum ether; thus, we obtained 10 g of 2, 6-dimethyl-Δ^3-cyclohexene-1-carboxylic acid (XVII) having a m.p. of 81-82°.

Found %: C 70.24, 70.05; H 9.13, 9.04. $C_9H_{14}O_2$. Calculated %: C 70.20; H 9.10.

In addition, we obtained 4 g of a liquid fraction having a b.p. of 140-145° at 25 mm.

Dehydrogenation and oxidation of the crystalline acid (XVII). 1 g of acid (XVII) (m.p. 81-82°), 0.8 g of 10% palladium on carbon and 20 ml of acetone were heated in an ampoule at 320° for 12 hours. The reaction product

was separated from the catalyst, the acetone was removed, and the residue was treated with a 10% solution of potassium hydroxide. The insoluble oil was extracted with ether. The ether extract was washed with water, the ether was removed, and the residue was boiled with a solution of 2 g of permanganate in 100 ml of water for 30 hours. After removing the manganese dioxide and acidifying the filtrate, we obtained 0.2 g of isophthalic acid having a m.p. of 330-335°, the dimethyl ester of which melted at 64-65° and did not give a depression of the m.p. with the known substance. After acidification of the alkaline extract, we obtained 0.1 g of an acid having a m.p. of 52-58° (from petroleum ether), the structure of which was not established.

Dehydrogenation and oxidation of the liquid mixture of acids (XVI) and (XVII). 1 g of the liquid fraction (b.p. 140-145° at 25 mm) described above, 0.8 g of 10% palladium on carbon and 20 ml of acetone were heated in an ampoule at 320° for 12 hours. The product was separated from the catalyst, the acetone was removed, and the residue was treated with a 10% solution of alkali. The alkaline layer was extracted with ether, the ether extract was washed with water and dried over magnesium sulfate. After removal of the ether, the oil remaining (0.3 g) was heated at 200° for one hour with 5 ml of 20% solution of nitric acid under a pressure of 30 atm of nitrogen. We obtained 0.2 g of isophthalic acid having a m.p. of 330-335°, the dimethyl ester of which melted at 64-65° and gave no m.p. depression with the known substance. On acidification of the alkaline extract, 0.16 g of 2,3-dimethylbenzoic acid (m.p. 142-143°) precipitated, and it also gave no m.p. depression with the known substance.

Ozonization of the crystalline acid (XVII). 5 g of the crystalline acid (XVII) (m.p. 81-82°) in a solution of 30 ml of 90% solution of acetic acid was ozonized at 0° for 6 hours (the ozone concentration was 6%). To the solution of the ozonide, 20 ml of hydrogen peroxide (30%) and 1.5 ml of sulfuric acid were added. The mixture was heated at 60-85° for 15 hours. Then 6 g of sodium acetate, acetic acid, an excess of hydrogen peroxide were added, the water was driven off, and the residue was extracted with absolute alcohol. The alcohol was removed, and the residue was recrystallized from a 5% solution of sulfuric acid. We obtained 2 g of 1,3-dimethyl-2-carboxyadipic acid (XVIII) having a m.p. of 182-183°.

Found %: C 49.89, 49.79; H 6.72, 6.77. $C_9H_{14}O_6$. Calculated %: C 50.20; H 6.80.

Hydrogenation of Methylethylethinylcarbinol

270 g of acetylene alcohol (b.p. 119-121°), obtained by condensing acetylene with methyl ethyl ketone [22], was hydrogenated with 1 g of 1% palladium on calcium carbonate. When 59 liters of hydrogen (58.2 theoretical liters) had been absorbed, the hydrogenation was stopped, and the product was distilled. We obtained 240 g of methylethylvinylcarbinol having a b.p. of 117-119°

Dehydration of Methylethylvinylcarbinol

30 g of the substance was passed at 310° over calcined magnesium sulfate for 4 hours. The reaction product was separated from the water layer and dried over magnesium sulfate; on distillation, we obtained 17 g of 1,2-dimethylbutadiene having a b.p. of 75-77°, n_D^{20} 1.4460.

By condensation of this diene with maleic anhydride, we obtained in a yield of 90% the corresponding addition product, which melted at 66-67° (from a mixture of petroleum ether and benzene).

Condensation of 1,2-Dimethylbutadiene with Acrylonitrile

10 g of 1,2-dimethylbutadiene (b.p. 75-77°), 6 g of acrylonitrile and 0.01 g of hydroquinone were heated at 210° for two hours. We obtained 11.2 g of a mixture of addition products (XIX) and (XX) having a b.p. of 122-125° at 25 mm, n_D^{20} 1.4765.

Found %: C 79.92, 79.98; H 9.54, 9.68. $C_9H_{13}N$. Calculated %: C 80.00; H 9.72.

Dehydrogenation and oxidation of the addition products (XIX) and (XX). 5 g of a mixture of the nitriles (XIX) and (XX) was passed over 5% palladium on carbon at 320° for two hours. We obtained 3.6 g of dehydrogenation products having a b.p. of 130-134° at 80 mm, n_D^{19} 1.5200.

3 g of the dehydrogenation products was boiled with 50 ml of 10% solution of sodium hydroxide for 12 hours. The reaction product was acidified with concentrated hydrochloric acid, and the acids which precipitated were separated. We obtained 1.2 g of a mixture of acids having a m.p. of 127-129°, which we did not succeed in separating by recrystallization. 0.9 g of this mixture of acids (m.p. 127-129°) was heated with 15 ml of 15% solution of nitric acid at 200° and a pressure of 30 atm of nitrogen for 3 hours. We obtained 0.7 g of hemimellitic acid having a m.p. of 195-196°, which did not give a m.p. depression with the known substance. We also separated 0.1 g of trimellitic acid having a m.p. of 228-230°* (in a sealed capillary), and its anhydride melted at 166-167°. A mixture

* For trimellitic acid, in the literature several very different melting points are given (225-230°, 228-230°, 235-238° in a closed capillary); such differences apparently are explained by the formation of the anhydride of this acid, which causes a decrease of the melting point.

of trimellitic acid and its anhydride was obtained, and neither with the respective known substances gave a m.p. depression. Moreover, 0.1 g of tetephthalic acid was obtained, and its dimethyl ester melted at 141-142° and gave no m.p. depression with the known substance.

Condensation of 1,2-Dimethylbutadiene with the Methyl Ester of Metacrylic Acid

21 g of 1,2-dimethylbutadiene (b.p. 75-77°), 28 g of methylmetacrylate and 0.01 g of hydroquinone were heated at 210° for 2 hours. We obtained 20 g of a mixture of the addition products (XXI) and (XXII) having a b.p. of 96° at 13 mm, n_D^{23} 1.4695.

Found %: C 73.12, 72.97; H 10.07, 10.12. $C_{11}H_{18}O_2$. Calculated %: C 72.53; H 9.88.

Saponification of the mixture of addition products (XXI) and (XXII). 20 g of the substance (b.p. 96° at 13 mm) and 50 ml of 20% solution of sodium hydroxide were boiled for 12 hours. The reaction product was acidified with 15 ml of concentrated hydrochloric acid, and the oil which separated was extracted with ether, dried over magnesium sulfate, and the residue again freed from ether and distilled in vacuo. We obtained 12 g of a mixture of the acids (XXIII) and (XXIV) having a b.p. of 151-162° at 12 mm, n_D^{23} 1.4805.

Found %: C 71.72, 71.60; H 9.67, 9.72. $C_{10}H_{16}O_2$. Calculated %: C 71.42; H 9.52.

Dehydrogenation and oxidation of the mixture of acids (XXIII) and (XXIV). 3.5 g of the substance (b.p. 151-152° at 12 mm) was dehydrogenated over 5% palladium on carbon at a temperature of 320-325°. We obtained 1.2 g of the isomeric trimethylbenzene (b.p. 160-170°, n_D^{20} 1.5020), which then was oxidized by 35 ml of 20% solution of nitric acid at 180-200° and a pressure of 30 atm of nitrogen for three hours. After concentrating the solution in vacuo, we obtained 1.2 g of a mixture of acids, separated by crystallization from a 10% solution of hydrochloric acid. We obtained 0.9 g of hemimellitic acid having a m.p. of 195-196°, which gave no depression of the m.p. with the known substance. Moreover, we isolated 0.15 g of trimellitic acid having a m.p. of 228-230°, the anhydride of which melted at 166-167°; both substances gave no depression with the known substances. We also obtained 0.05 g of terephthalic acid having a m.p. of 300°, the dimethyl ester of which melted at 141-142° and gave no depression with the known substance.

Condensation of Vinylcyclohexene and Acrylonitrile

13.5 g of vinylcyclohexene (m.p. 141-142°), 7.8 g of acrylonitrile (b.p. 78°) and 0.01 g of hydroquinone were heated in an ampoule at 230° for two hours. After distillation in vacuo, we obtained 19 g of a mixture of the addition products (XXV) and (XXVI) having a b.p. of 154-155° at 22 mm, n_D^{23} 1.5010. On distilling a second time, a product having a b.p. of 162° at 26 mm, n_D^{20} 1.5024 was obtained.

Found %: C 81.93, 81.73; H 9.46, 9.38. $C_{11}H_{15}N$. Calculated %: C 82.00; H 9.32.

Dehydrogenation and saponification of the mixture of addition products (XXV) and (XXVI). 5 g of the substance was passed at 320° over 5% palladium on carbon for 5.5 hours. We obtained 3.6 g of dehydrogenation products (b.p. 160-175° at 27 mm, n_D^{20} 1.5830), which was then boiled with 10 ml of 30% solution of sodium hydroxide for 20 hours. The reaction product was extracted with ether, the aqueous layer was acidified with hydrochloric acid, and the mixture of acids obtained was separated. After recrystallization from methanol and toluene, we obtained 1.8 g of α-naphthoic acid having a m.p. of 164-165°, and not giving a depression of the m.p. with the known substance. Moreover, we separated 0.1 g of β-naphthoic acid having a m.p. of 181-182°, which also gave no m.p. depression with the known substance, obtained by the oxidation of β-methylnaphthalene.

Oxidation of β-methylnaphthalene. 3 g of β-methylnaphthalene and 40 ml of 12% solution of nitric acid were heated at 200° under a pressure of 20 atm of nitrogen for 3 hours. We obtained 1.5 g of β-naphthoic acid having a m.p. of 183-184° (from toluene).

Condensation of Isoprene with the Methyl Ester of Metacrylic Acid

50 g of methylmetacrylate (b.p. 100-101°), 30 g of isoprene and 0.1 g of hydroquinone were heated in a metal ampoule at 220° for two hours. The reaction product was distilled in vacuo with a column of 20 theoretical plates. We obtained 52 g of a mixture of addition products (XXVII) and (XXVIII) in the form of a pleasant-smelling liquid having a b.p. of 80.5° at 11 mm, n_D^{20} 1.4595.

Found %: C 71.77, 71.96; H 9.56, 9.64. $C_{10}H_{16}O_2$. Calculated %: C 71.50, 71.96; H 9.53, 9.64.

Saponification of the mixture of addition products (XXVII) and (XXVIII). 90 g of the substance (b.p. 80.5° at 11 mm) was boiled for 1 hour with a solution of 120 ml of 40% sodium hydroxide. The reaction product was acidified with 120 ml of concentrated HCl, and then the oil which separated was extracted with ether. The

ether extract was dried over magnesium sulfate, the ether was removed, and the residue was distilled in vacuo. We obtained 70 g of a mixture of the acids (XXIX) and (XXX) having a b.p. of 131° at 12 mm, n_D^{20} 1.4770. On standing, this mixture partially crystallized. The crystals were separated and recrystallized from 50% methanol. We obtained 30 g of 1,4-dimethyl-Δ^1-cyclohexene-4-carboxylic acid (XXX) having a m.p. of 62-63°.

Found %: C 70.12, 70.05; H 9.10, 8.92. M 150.2, 143.4 (titration). $C_9H_{14}O_2$. Calculated %: C 70.20; H 9.10. M 154.

The 40 g residue, after separation of the crystallizing acid (XXX), represents a liquid mixture of acids (XXIX) and (XXX), in which, as shown below, the acid of the para-structure (XXX) predominates.

Production of the amide from the crystalline acid (XXX). 1 g of the acid (XXX) (m.p. 62-63°) and 1 ml of thionyl chloride were heated at 40° for 3 hours. The excess of thionyl chloride was removed in vacuo, and the remaining acid chloride was added dropwise to a cooled and stirred 5 ml of concentrated ammonia solution. After recrystallization from water, 0.7 g of the amide having a m.p. of 113-114°, was obtained.

Found %: N 9.38, 9.40. $C_9H_{15}ON$. Calculated %: N 9.15.

Production of the amides from the liquid mixture of acids (XXIX) and (XXX). 10 g of a liquid mixture of acids (b.p. 131° at 12 mm) and 10 ml of thionyl chloride were heated at 40° for 3 hours. The excess of thionyl chloride was removed in vacuo, and the residue distilled. We obtained 8 g of acid anhydrides, having a b.p. of 97-102° at 12 mm, which was added dropwise, with mixing, to an ice-cold concentrated solution of ammonia (45 ml). As a result of fractional crystallization from water, we obtained 5 g of the amide of the acid (XXX) having a m.p. of 113-114°, and not giving a m.p. depression with the substance described above. Moreover, we separated 1 g of the amide of the isomeric acid (XXIX) having a m.p. of 49-50°.

Found %: N 9.23, 9.31. $C_9H_{15}ON$. Calculated %: N 9.15.

Saponification of the amide of the acid (XXIX). 4.5 g of the amide (m.p. 49-50°) was boiled with 35 ml of a 15% solution of sodium hydroxide for 16 hours. The reaction product was extracted with ether, and the aqueous layer was acidifted with 25 ml of concentrated hydrochloric acid. The oil that separated was extracted with ether, dried over magnesium sulfate and distilled in vacuo. We obtained 2 g of liquid acid (XXIX) having a b.p. of 125° at 9 mm, n_D^{20} 1.4740.

Found %: C 69.38, 69.90; H 8.99, 8.90. $C_9H_{14}O_2$. Calculated %: C 70.20; H 9.10.

Dehydrogenation and oxidation of the liquid acid (XXIX). 2 g of the liquid acid (XXIX) having a b.p. of 125° at 9 mm was dehydrogenated over 5% palladium on carbon at a temperature of 305° for 2 hours. We obtained 0.8 g of m-xylene (n_D^{20} 1.4910), which was oxidized by 30 ml of 20% solution of nitric acid at 200° under a pressure of 25 atm of nitrogen for 2 hours. The isophthalic acid separating was isolated from the solution and recrystallized from hot water; thus, we obtained 0.5 g of isophthalic acid in the form of characteristic needles having a m.p. of 330-335°, the dimethyl ester of which melted at 64-65° and gave no depression of the m.p. with the known substance.

Oxidation of a mixture of commercial xylenes and separation of the phthalic acid formed. 2.7 g of a mixture of xylenes (b.p. 130-135°), 21 g of chromic anhydride, 180 ml of 50% acetic acid solution and 30 ml of concentrated sulfuric acid were refluxed for 3 hours. The reaction product was diluted twice with water. The mixture of acids obtained was separated, washed with water and dried. The acids obtained in a quantity of 1 g were mixed with 2 ml of concentrated solution of ammonia, the mixture was refluxed for a half-hour and diluted to 3.5 ml. The aqueous solution was boiled on the water bath until the disappearance of the odor of ammonia. To the boiling solution (3.5 ml) we added a solution of 0.6 g of barium chloride in 4.5 ml of water, and the liquid was heated to boiling. Barium terephthalate precipitated from the cooled solution, and was then separated and boiled with 2 ml of concentrated hydrochloric acid solution. The terephthalic acid obtained (0.15 g) was converted to the dimethyl ester having a m.p. of 141-142°, which gave no m.p. depression with the known substance. The filtrate, after separation of the barium terephthalate, was diluted to 50 ml with water, acidified with hydrochloric acid and heated to boiling. The isophthalic acid (0.6 g) which separated on cooling melted (in a closed capillary) at 330-332°, and the dimethyl ester melted at 64-65° and also gave no m.p. depression with the known substance.

Dehydrogenation and oxidation of the crystalline acid (XXX). 5 g of the acid (XXX) (m.p. 62-63°) was dehydrogenated over 5% palladium on carbon at 305° for 2 hours. We obtained 2 g of p-xylene (b.p. 130-139, n_D^{20} 1.4885), which then was oxidized by a solution of 16 g of chromic anhydride in 40 ml of water, 40 ml of acetic acid and 20 ml of concentrated sulfuric acid. The mixture was refluxed for 2.5 hours. The reaction product was diluted twice, the acid which separated was filtered off, washed with cold water and dried at 100°. We obtained 1.45 g of terephthalic acid, from which, by heating with methanol (15 ml) in the presence of concentrated sulfuric acid (15 ml), we obtained 1.2 g of the dimethyl ester having a m.p. of 141-142° (from methanol), which gave no m.p. de-

pression with the known dimethyl ester of terephthalic acid.

Dehydrogenation and oxidation of the liquid mixture of acids (XXIX) and (XXX). 5 g of the substance (b.p. 131° at 12 mm) was dehydrogenated at 300° over 5% palladium on carbon for 3 hours. We obtained 2.5 g of a mixture of acids (b.p. 130-138°; n_D^{17} 1.4930) which was oxidized by boiling with a solution of 20 g of chromic anhydride in 120 ml of 50% solution of acetic acid and 20 ml of sulfuric acid for 3 hours. The reaction product was diluted twice with water, and the phthalic acid (1.25 g) separating was isolated, as described above. We obtained 1 g of terephthalic acid and 0.3 g of isophthalic acid, the dimethyl esters of which melted at 141-142° and 64-65°, respectively, and gave no m.p. depressions with the respective known substances.

Ozonization of the crystalline acid (XXX). 5 g of the acid (m.p. 62-63°) was ozonized in a solution of 50 ml of 90% acetic acid at 0° for 6 hours (ozone concentration 5%). To the solution of the ozonide, 10 ml of a 70% solution of peracetic acid was added, and the mixture was refluxed at 60-65° for 15 hours. The acetic and peracetic acids were removed in vacuo. We obtained 4 g of an oil, which on standing, partially crystallized. The crystals were separated, washed with ether and recrystallized from 10% solution of hydrochloric acid. We obtained 1.8 g of 2-methyl-2-carboxyadipic acid (XXXI) having m.p. of 126-127°, which gave no m.p. depression with the known compound.

Condensation of Isoprene with the Methyl Ester of Acrylic Acid

19 g of isoprene, 23 g of methyl acrylate (b.p. 78-79°) and 0.05 g of hydroquinone were heated in an ampoule at 100° for 10 hours. The reaction product was distilled in vacuo; thus, we obtained 30 g of a mixture of addition products (XXXII) and (XXXIII) having a b.p. of 86° at 12 mm, n_D^{23} 1.4610.

Saponification of the mixture of addition products (XXXII) and (XXXIII). 14 g of the substance (b.p. 86° at 12 mm) was boiled, using a reflux condenser, with 70 ml of a 15% solution of potassium hydroxide for 3 hours. The product was acidified with 40 ml of concentrated hydrochloric acid, the mixture of acids separating was isolated, extracted with ether, dried over magnesium sulfate and distilled in vacuo. We obtained 10 g of liquid mixture of acids (XXXIV) and (XXXV) having a b.p. of 155-160° at 39 mm, from which we isolated 7 g of crystalline 1-methyl-Δ^1-cyclohexene-4-carboxylic acid (XXXIV) having a m.p. of 83-84 (from aqueous methanol).

Found %: C 68.52, 68.57; H 8.91, 9.00; $C_8H_{12}O_2$. Calculated %: C 68.54; H 8.63.

Dehydrogenation of the crystalline acid (XXXIV). 1 g of the substance (m.p. 83-84°), 50 ml of benzene and 0.5 g of 5% palladium on carbon were heated at 300° for 12 hours. We obtained 0.3 g of p-toluic acid having m.p. of 179-180° (from alcohol). A mixture of the sample with the known substance failed to depress the melting point.

Dehydrogenation of the mixture of addition products (XXXII) and (XXXIII). 4.5 g of the substance (b.p. 86° at 12 mm) was passed at 320° over 5% palladium on carbon for 3 hours. We obtained 2.7 g of dehydrogenation product (b.p. 90.5° at 12 mm, n_D^{23} 1.4970), which was saponified by 30 ml of 10% solution of potassium hydroxide by boiling, employing a reflux condenser, for 4 hours. The reaction product was acidified by hydrochloric acid, the mixture of acids separating was isolated and recrystallized from 50% methanol. We obtained 1.8 g of p-toluic acid having m.p. of 178-179°, which gave no depression of m.p. when mixed with the known substance, and we obtained 0.2 g of m-toluic acid, having m.p. of 109-110°. The latter was oxidized to phthalic acid, the dimethyl ester of which melted at 64-65° and also gave no m.p. depression with the known substance.

Synthesis of Methyl-tert-butylethinylcarbinol

Into a three-necked flask, provided with a stirrer, we placed 170 g of powdered potassium hydroxide and 1600 ml of dry ether. The mixture was saturated for 1.5 hours with acetylene at −10°, then with intense stirring, in the current of acetylene, we added 212 g of pinacolin dropwise. The passage of acetylene was continued for 1.5 hours more until completion of the addition of the ketone. The reaction product was treated with 600 ml of water containing ice. The ether layer was separated, washed with 5% hydrochloric acid solution and a solution of sodium bicarbonate, and dried over magnesium sulfate. We obtained 205 g of methyl-tert-butylethinylcarbinol having a b.p. of 140-142°, n_D^{23} 1.4352 [18].

Hydrogenation of Methyl-tert-butylethinylcarbinol

86 g of the substance was hydrogenated in the presence of palladium on calcium carbonate. After absorbing 17.6 liters of hydrogen (the theoretical is 17 liters) the hydrogenation was discontinued, and the reaction product was distilled. We obtained 80 g of methyl-tert-butylvinylcarbinol having a b.p. of 65-67° at 62 mm, n_D^{21} 1.4354.

Dehydration of Methyl-tert-butylvinylcarbinol

21.3 g of vinyl alcohol (b.p. 65-67° at 62 mm) was passed over calcined magnesium sulfate at 320-330° for two hours. We obtained 12 g of 2-tertiary butylbutadiene having a b.p. of 103-105°, n_D^{23} 1;4208.

Condensation of 2-tert-butylbutadiene with Methyl Methacrylate

4 g of the diene (b.p. 103-105°), 4 g of methyl methacrylate and 0.01 g of hydroquinone were heated in an ampoule at 230° for 1.5 hours. We obtained 2.8 g of the addition product (XXXVII) having a b.p. of 118-120° at

20 mm, n_D^{18} 1.4620.

Found %: C 72.39, 72.18; H 10.23, 10.46. $C_{13}H_{22}O_2$. Calculated %: C 74.30; H 10.23.

Saponification of the addition product (XXXVII). 12 g of the substance (b.p. 118-120° at 20 mm) was boiled 2 hours with 35 ml of a 30% solution of sodium hydroxide. The reaction product was acidified with concentrated hydrochloric acid (27 ml) and extracted with ether. The ether was removed, and the residue was recrystallized from 50% methanol. We obtained 8.7 g of 1-tert-butyl-4-methyl-Δ^1-cyclohexene-4-carboxylic acid (XXXVIII) having a m.p. of 87.5° (from water).

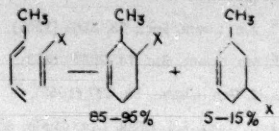
Found %: C 73.35, 73.16; H 10.76, 10.63. $C_{12}H_{20}O_2$. Calculated %: C 73.47; H 10.21.

Dehydrogenation and oxidation of the acid (XXXVIII). 2 g of the substance (m.p. 87.5°) was dehydrogenated at 310° over 5% palladium on carbon. We obtained 1 g of dehydrogenation product (n_D^{27} 1.4871), which was oxidized by boiling with 10 g of chromic anhydride in a solution of 60 ml of 50% acetic acid solution and 10 ml of concentrated sulfuric acid for 2 hours. The reaction product was diluted with water, the p-tert-butylbenzoic acid separating (0.75 g) was isolated, and after recrystallization from water, melted at 166.5-167°. The substance gave no m.p. depression with known p-tert-butylbenzoic acid.

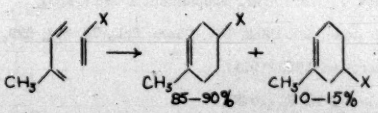
SUMMARY

1. We systematically investigated the structural directability of the diene condensation of asymmetric substituted dienes (pentadiene, isoprene, 1,2-dimethylbutadiene and 1-vinyl-Δ^1-cyclohexene) with asymmetric dienophiles (acrylonitrile, methylacrylate, methyl metacrylate, crotonic acid, styrene).

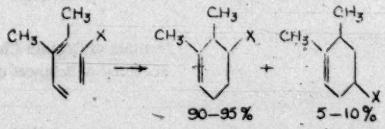
2. The condensation of trans-pentadiene with asymmetric dienophiles, in all cases, gave a mixture of addition products, containing 85-95% of the ortho-isomer and 5-15% of the meta-isomer.



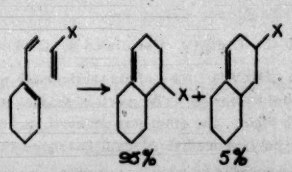
3. The condensation of isoprene with asymmetric dienophiles also in all cases led to the formation of a mixture of addition products, containing 85-90% of the para-isomer and 10-15% of the meta-isomer:



4. The structural directability of the diene condensation of 1,2-dimethylbutadiene with asymmetric dienophiles has the same character as pentadiene; thus, a mixture of addition products, containing 90-95% of the ordinary ortho-isomer and 5-10% of the rarer meta-isomer, formed:



5. The diene condensation of vinylcyclohexene with asymmetric dienophiles leads still further to the mono-structure and leads to formation of a mixture of addition products, which contain about 95% of the ortho-isomer and only about 5% of the meta-isomer:



6. The structures of the addition products, in all cases, were rigorously established by a combination of accurate fractional distillation, dehydrogenation, and new methods of oxidation and ozonization.

LITERATURE CITED

[1] K. Alder, W. Vogt, Ann., 564, 120 (1949).

[2] J. Meek, F. Lorenzi, S. Cristol, J. Am. Chem. Soc., 71, 1820 (1949).

[3] G. Ropp. E. Coyner, J. Am. Chem. Soc., 71, 1033 (1949).

[4] R. Frank, R. Emmick, R. Johnson, J. Am. Chem. Soc., 69, 2213 (1947).

[5] J. Meek, J. Rangsdale, J. Am. Chem. Soc., 70, 2502 (1948).

[6] B. A. Arbuzov, E. G. Kataev, J. Gen. Chem., 20, 68 (1950).*

[7] K. Alder, W. Vogt, J. Haydn, Ber., 86, 1312 (1953); K. Alder, K. Heimbach, E. Kühle, Ber., 86, 1364 (1953).

[8] K. Alder, W. Vogt, Ann., 564, 109 (1949).

[9] J. Meek, K. Merrow, D. Ram y, J. Am. Chem. Soc., 73, 5563 (1951).

[10] J. Meek, K. Merrow, S. Cristol, J. Am. Chem. Soc, 74, 2667 (1952).

[11] I. N. Nazarov and T. D. Nagibina, J. Gen. Chem., 23, 577 (1953).**

[12] I. N. Nazarov and I. V. Torgov, Bull. Acad. Sci. USSR, Div. Chem. Sci., 1074 (1953).***

[13] E. Bengtsson, British Patent 662229, 5 XII, 1953.

[14] A. Bofors, British Patent 662139, 5 XII, 1951.

[15] E. Bengtsson, Acta. chem. Scandinavica, 7, 774 (1953).

[16] A. A. Petrov and N. P. Sopov, J. Gen. Chem., Supplement I, 369 (1953).

[17] I. N. Nazarov, et. al., Bull. Acad. Sci. USSR, Div. Chem. Sci., 78, 901, 920, 929, 1076 (1953).****

[18] M. Smith, J. Am. Chem. Soc., 43, 1920 (1921).

[19] I. A. Favorskaya, J. Gen. Chem., 18, 52 (1948).

[20] I. N. Nazarov, et. al., Bull. Acad. Sci. USSR, Div. Chem. Sci., 78 (1953).*****

[21] R. Linstead, K. Michaelis, S. Thomas, J. Chem. Soc., 1940, 1138.

[22] I. N. Nazarov, I. L. Kotlyarevsky and V. F. Ryabchenko, J. Gen. Chem., 23, 1900 (1953).******

Received July 26, 1954

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Academy of Sciences of the USSR

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* See Consultants Bureau Translation, page 73.
** See Consultants Bureau Translation, page 599.
*** See Consultants Bureau Translation, pages 955.
**** See Consultants Bureau Translation, page 69, 799, 817, 827, 935.
***** See Consultants Bureau Translation, page 69.
****** See Consultants Bureau Translation, page 2011.

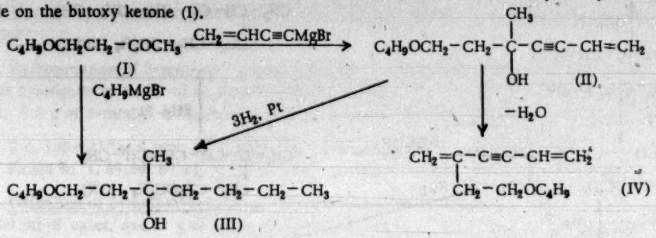
162. SYNTHESIS AND TRANSFORMATIONS OF METHYLBUTOXYETHYLVINYLETHYNYLCARBINOL

S. A. Vartanyan, V. N. Zhamagortsyan, and I. N. Nazarov

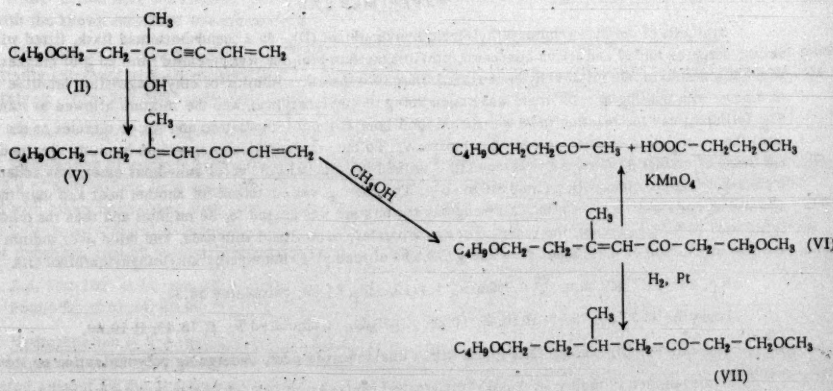
In the previous communication [1] the transformations of methyl-β-ethoxyethylvinylethyny carbinol were described, which compound was synthesized by the condensation of vinylacetylenemagnesium bromide with methyl-β-methoxyethyl ketone. It was interesting to elucidate the influence of the butoxy group on the transformations of vinyl ethynylcarbinols. With this in mind we studied the condensation of vinylacetylene with methyl β-butoxyethyl ketone (I), which was readily obtained by the hydration of vinylacetylene in butyl alcohol:

$$CH_2{=}CH{-}C{\equiv}CH \xrightarrow[H_2O]{C_4H_9OH} CH_3{-}CO{-}CH_2{-}CH_2OC_4H_9 \quad (I)$$

The reaction between vinylacetylenemagnesium bromide and the butoxy ketone (I) is normal and leads to the formation of methyl-β-butoxyethylvinylethynylcarbinol (II) in excellent yield. In the hydrogenation of carbinol (II) with Pt catalyst in ethyl alcohol the amount of hydrogen absorbed is 3 moles and the compound methyl-β-butoxy-ethylbutylcarbinol (III) is obtained. The latter was also obtained in about 53% yield by the action of butylmagnesium bromide on the butoxy ketone (I).



Under the influence of mercuric sulfate in methanol solution, the carbinol (II), similar to other vinylethynyl-carbinols [2], isomerizes into 3-methyl-1-butoxy-3,6-heptadien-5-one (V), which, under the experimental conditions, adds 1 mole of methanol at the unsubstituted vinyl group to give 3-methyl-7-methoxy-1-butoxyhepten-5-one (VI).



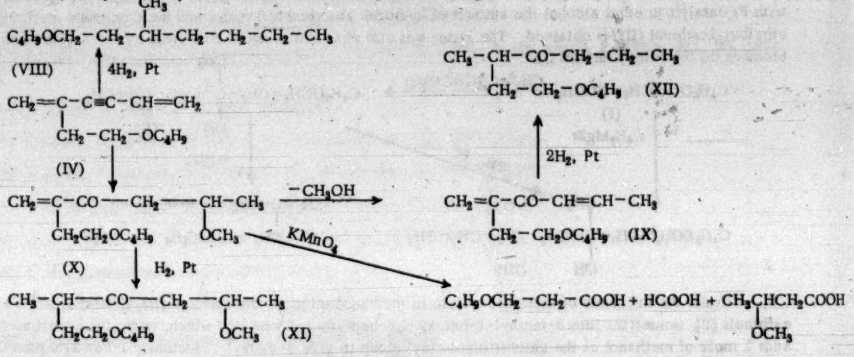
When hydrogenated with Pt catalyst the dialkoxy ketone (VI) absorbs 1 mole of hydrogen and is transformed into 3-methyl-1-butoxy-7-methoxyheptan-5-one (VII). Attempts to cleave methanol from the ketone (VI) proved unsuccessful; instead, a mixture of products was obtained fromwhich an individual substance could not be isolated.

The structure of the alkoxy ketone (VI) was definitely established by oxidation, which gave β-methoxypropionic acid [3] and methyl-β-butoxyethyl ketone, identified by taking a mixed melting point of the 2,4-dinitrophenylhydrazone with the known substance.

Under the influence of 50% sulfuric acid at 65-70° for 2 hours the alkoxycarbinol (II) suffers complete dehydration with the formation of 2-β-butoxyethyl-1,5-hexadien-3-yne (IV) (yield about 65%).

When hydrogenated in alcohol solution in the presence of Pt catalyst the dienyne (IV) absorbs 4 moles of hydrogen and is transformed into 1-butoxy-3-methylheptane (VIII).

Analogous to other dienynes [4], the hydration of the dienyne (IV) in 90% methanol in the presence of sulfuric acid and mercuric sulfate for 29 hours gives 2-β-butoxyethyl-1,4-hexadien-3-one (IX), which, under the experimental conditions, adds 2 mole of methanol to form 5-methoxy-2-β-butoxyethyl-1-hexen-3-one (X). 2-β-Butoxyethyl-1,4-hexadien-3-one (IX) was obtained by the vacuum distillation of ketone (X) in the presence of p-toluenesulfonic acid. In the hydrogenation of the alkoxy ketone (X) in alcohol solution in the presence of Pt catalyst 1 mole of hydrogen is absorbed and the compound 3-methyl-6-methoxy-1-butoxyheptan-4-one (XI) is formed. Under analogous conditions the dienone (IX) absorbs 2 moles of hydrogen and gives 8-methyl-1-butoxyheptan-4-one (XII). The structure of the alkoxy ketone (X) was proven by oxidation, the oxidation products being β-methoxybutyric, formic and β-butoxypropionic acids.



EXPERIMENTAL

Synthesis of methyl-β-butoxyethylvinylethynylcarbinol (II). In a round-bottomed flask, fitted with mechanical stirrer, dropping funnel and reflux condenser, ethylmagnesium bromide was prepared from 65 g of magnesium and 300 g of ethyl bromide in 500 ml of anhydrous ether. Then into the ether solution of ethylmagnesium bromide over a period of 5 hours with cooling to −18° there was passed 200 g of vinylacetylene, and the mixture allowed to stand overnight. The following day the reaction mass was stirred for 1 hour at room temperature and for 40 minutes at the b.p. of ether until the evolution of ethane had ceased completely. To the vinylacetylenemagnesium bromide obtained in this manner 230 g of methyl β-butoxyethyl ketone (I), dissolved in an equal volume of anhydrous ether, was added dropwise over a period of 6 hours with cooling (from −16 to +8°). The stirring was continued for another hour and then the mixture was allowed to stand overnight. On the following day the mixture was heated for 30 minutes and then the product was hydrolyzed with 10% HCl solution, the ether layer was separated, neutralized with soda, and dried over sodium sulfate. The vacuum distillation of the product gave 280 g (73.5%) of methyl-β-butoxyethylvinylethynylcarbinol (II).

B.p. 109-111° at 4 mm, d_4^{20} 0.9092, n_D^{20} 1.4713, MR_D 61.26; calculated 58.31.

Found %: C 73.60, 73.73; H 10.46, 10.20. $C_{12}H_{20}O_2$. Calculated %: C 73.47; H 10.20.

The carbinol (II) is a colorless liquid with a characteristic odor, undergoing polymerization on standing.

Hydrogenation of methyl-β-butoxyethylvinylethynylcarbinol (II). 3 g of freshly distilled carbinol (II) was hydrogenated in 10 ml of alcohol in the presence of Pt catalyst. 1.2 liters of hydrogen was absorbed instead of the calculated

1.1 liters. 2.5 g of methyl-β-butoxyethylbutylcarbinol (III) was obtained as a colorless liquid with a characteristic odor.

B.p. 104° at 4 mm, d_4^{20} 0.8688, n_D^{20} 1.4390, MR_D 61.17; calculated 60.78.
Found %: C 71.65, 71.48; H 13.03, 13.13. $C_{12}H_{26}O_2$. Calculated %: C 71.29; H 12.87.

Action of butylmagnesium bromide on methyl β-butoxyethyl ketone. In a round-bottomed flask butylmagnesium bromide was prepared in the usual manner from 2.6 g of magnesium and 15 g of butyl bromide in 30 ml of anhydrous ether. Then, with ice water cooling and constant stirring, 10 g of the butoxy ketone (I) in 15 ml of anhydrous ether was added dropwise. The stirring was continued for another hour at 25°, after which the product was hydrolyzed with 8% HCl solution, extracted with ether, dried over sodium sulfate, and vacuum distilled. 7.4 g of the above described methyl-β-butoxyethylbutylcarbinol (III) was obtained, b.p. 108° at 6 mm, n_D^{20} 1.4400.

Isomerization of methyl-β-butoxyethylvinylethynylcarbinol (II). A mixture of 86 g of freshly distilled carbinol (II), 258 g of distilled methanol, 3 g of finely divided mercuric sulfate and a small amount of pyrogallol was stirred for 8 hours at 35 - 40°. During this period another 7 g of mercuric sulfate was added. At the start the temperature of the reaction mass was raised to 50°; then heating was terminated due to the exothermic nature of the reaction, and toward the end of the reaction the mixture was heated again on the water bath. The reaction product was decanted from the catalyst, carefully neutralized with soda solution, dried over sodium sulfate, and distilled in vacuo. 58.3 g of 3-methyl-7-methoxy-1-butoxy-3-hepten-5-one (VI) was obtained as a light yellow mobile liquid with a characteristic odor.

B.p. 142-143° at 6 mm, d_4^{20} 0.9429, n_D^{20} 1.4598, MR_D 66.26; calculated 65.06.
Found %: C 68.23, 68.11; H 10.80, 10.75. $C_{13}H_{24}O_3$. Calculated %: C 68.42; H 10.52.

The alkoxy ketone (VI) failed to give crystalline derivatives with semicarbazide and 2,4-dinitrophenylhydrazine.

Hydrogenation of 3-methyl-7-methoxy-1-butoxy-3-hepten-5-one (VI). 4 g of freshly distilled alkoxy ketone (VI) was hydrogenated in 15 ml of alcohol with Pt catalyst. 500 ml of hydrogen was absorbed instead of the calculated 410 ml. 3.3 g of 3-methyl-7-methoxy-1-butoxyheptan-5-one (VII) was obtained as a clear mobile liquid.

B.p. 130-131° at 6 mm, d_4^{20} 0.9212, n_D^{20} 1.4404, MR_D 65.82, calculated 65.53.
Found %: C 67.38, 67.87; H 11.56, 11.67. $C_{13}H_{26}O_3$. Calculated %: C 67.82; H 11.30.

Oxidation of 3-methyl-7-methoxy-1-butoxy-3-hepten-5-one (VI). 10 g of the alkoxy ketone (VI) was mixed with 200 ml of water, and 21 g of finely divided potassium permanganate was added in small portions over a period of 4 hours with constant stirring. The reaction mass was allowed to stand overnight, and on the following day it was again stirred for 3 hours. The manganese dioxide was removed by filtration, washed with hot water, the neutral products extracted with ether, dried over sodium sulfate, and distilled. 2 g of methyl β-butoxyethyl ketone was obtained, b.p. 177-181° at 680 mm, n_D^{20} 1.4215. The 2,4-dinitrophenylhydrazone of this ketone had m.p. 211-212° and the mixed m.p. with the known substance was not depressed.

The aqueous solution of salts was acidified with concentrated hydrochloric acid (10 ml), the organic acids were exhaustively extracted with ether, dried over sodium sulfate, and distilled in vacuo. 2 g of β-methoxypropionic acid was obtained, b.p. 200-202° at 678 mm, n_D^{20} 1.4204. The silver salt of the acid was prepared.

Found %: Ag 50.94. $C_4H_7O_3Ag$. Calculated %: Ag 51.18.

Dehydration of methyl-β-butoxyethylvinylethynylcarbinol (II). A mixture of 136 g of the butoxycarbinol (II) and 135 g of 50% sulfuric acid was vigorously stirred on the water bath at 68-70° for 2 hours. The product was extracted with ether, neutralized with soda solution, washed with water, dried over sodium sulfate, and distilled in vacuo. 80 g of 2-β-butoxyethyl-1,5-hexadien-3-yne (IV) was obtained as a light yellow mobile liquid, which, on standing, without stabilizer, rapidly polymerizes, at first into a viscous mass, and then into a solid polymer.

B.p. 100-102° at 10 mm, d_4^{20} 0.8612, n_D^{20} 1.4320. MR_D 59.96; calculated 56.32.
Found %: C 81.34, 80.95; H 10.35, 10.23. $C_{12}H_{18}O$. Calculated %: C 80.90; H 10.11.

Hydrogenation of 2-β-butoxyethyl-1,5-hexadien-3-yne (IV). 3 g of freshly distilled butoxydienyne (IV) was hydrogenated in 15 ml of alcohol in the presence of platinum oxide. 1.8 liters of hydrogen was absorbed; the calculated amount for the hydrogenation of two double and one triple bond is 1.65 liters of hydrogen. 2.5 g of 1-butoxy-3-methylheptane was obtained as a colorless, mobile liquid with a characteristic odor.

B.p. 87° at 9 mm, d_4^{20} 0.7979, n_D^{20} 1.4259, MR_D 59.71; calculated 59.26.
Found %: C 76.71, 76.64; H 14.02, 14.39. $C_{12}H_{26}O$. Calculated %: C 77.42; H 13.98.

Hydration of 2-β-butoxyethyl-1,5-hexadien-3-yne (IV). To 650 g of 90% methanol was added 4 g of mercuric sulfate, 1 ml of concentrated sulfuric acid and 160 g of pyrogallol-stabilized dienyne (IV) (b.p. 99-103° at 7 mm, n_D^{20} 1.4845). The mixture was vigorously stirred at 62-65° for 29 hours. During this time another 28 g of mercuric sulfate was added in small portions. The main portion of the methanol was removed by distillation in vacuo (about 60 mm) at 45-50°. The product was well neutralized with soda, extracted with ether, dried over sodium sulfate, and distilled in vacuo. 83 g of the dialkoxy ketone (X) was obtained in admixture with the dienone (IX); b.p. 116-137° at 10 mm, n_D^{20} 1.461, and 24 g of the dienyne (IV), b.p. 103-110° at 10 mm, n_D^{20} 1.4890. Further fractional distillation gave pure 5-methoxy-2-β-butoxyethyl-1-hexen-3-one (X) as a clear, mobile liquid.

B.p. 126-129° at 4 mm, d_4^{20} 0.9403, n_D^{20} 1.4576, MR_D 65.96; calculated 65.06.
Found %: C 68.71, 68.57; H 11.02, 11.02. $C_{13}H_{24}O_3$. Calculated %: C 68.42; H 10.52.

Hydrogenation of 5-methoxy-2-β-butoxyethyl-1-hexen-3-one (X). 2.6 g of freshly distilled ketone (X) was hydrogenated in 10 ml of alcohol with Pt catalyst. 280 ml of hydrogen was absorbed instead of the calculated 273 ml. 2.1 g of 3-methyl-6-methoxy-1-butoxyheptan-4-one (XI) was obtained.

B.p. 119-120° at 5 mm, d_4^{20} 0.9149, n_D^{20} 1.4389, MR_D 66.14; calculated 65.53
Found %: C 67.63; H 11.49. $C_{13}H_{26}O_3$. Calculated %: C 67.82; H 11.30.

Oxidation of 5-methoxy-2-β-butoxyethyl-1-hexen-3-one (X). To 15 g of the butoxy ketone (X) in 200 ml of water was added 29 g of finely powdered potassium permanganate in small portions over a period of 5 hours with vigorous stirring and water cooling. The following day the mixture was stirred another 2 hours at room temperature. On conclusion of oxidation, the manganese dioxide was removed by filtration and thoroughly washed with hot water. The solution of salts was extracted with ether to remove neutral substances, but hardly any were found to be present.

The water solution of organic acid salts was evaporated on the water bath, the residue was acidified with concentrated hydrochloric acid (11 ml), the separated acids were extracted with ether, dried over sodium sulfate, and distilled in vacuo:

First fraction 60-67° at 130 mm, 1.6 g; second fraction 106-108° at 11 mm, 2.1 g; third fraction 116-118° at 6 mm, 1.8 g, n_D^{20} 1.4313.

After drying over sodium sulfate, the first fraction was distilled at atmospheric pressure, b.p. 98-100° at 680 mm. The calomel test was positive (formic acid).

The second fraction is β-methoxybutyric acid, b.p. 109-111° at 13 mm, n_D^{20} 1.4214. Its silver salt was obtained.

Found %: Ag 48.33. $C_5H_9O_3Ag$. Calculated %: Ag 48.0.

The third fraction is β-butoxypropionic acid, b.p. 116-118° at 6 mm, n_D^{20} 1.4270 (from the literature, b.p. 93.5-95° at 2 mm, n_D^{20} 1.4264 [5]).

Cleavage of methanol from 5-methoxy-2-β-butoxyethyl-1-hexen-3-one (X). 20 g of the alkoxy ketone (X), after heating for 30 minutes to 105°, was vacuum distilled at 15 mm, in the presence of 0.1 g of p-toluenesulfonic acid. The reaction product was redistilled twice to give 6 g of 2-β-butoxyethyl-1,4-hexadien-3-one (IX).

B.p. 109-110° at 4 mm, n_4^{20} 0.9292, n_D^{20} 1.4700, MR_D 58.85; calculated 58.34.
Found %: C 72.05; H 10.65. $C_{12}H_{20}O_2$. Calculated %: C 73.47; H 10.20.

Hydrogenation of 2-β-butoxyethyl-1,4-hexadien-3-one (IX). 2.6 g of the butoxydienone (X) was hydrogenated in 10 ml of alcohol in the presence of platinum oxide. 0.7 liters of hydrogen was absorbed; theory for the hydrogenation of two double bonds is 0.637 liters. 2 g of 3-methyl-1-butoxyheptan-4-one (XII) was obtained.

B.p. 93-94° at 4 mm, d_4^{20} 0.8567, n_D^{20} 1.4335, MR_D 59.56; calculated 59.27.
Found %: C 72.00; H 12.98. $C_{12}H_{24}O_2$. Calculated %: C 72.00; H 12.00.

SUMMARY

The action of vinylacetylenemagnesium bromide on methyl β-butoxyethyl ketone (I) gave methyl-β-butoxyethylvinylethynylcarbinol (II), which, under the influence of mercuric sulfate in methanol solution, isomerizes into the corresponding divinyl ketone (V), while the latter, under the experimental conditions adds 1 mole of methanol to give the ketone (VI), containing both the methoxyl and butoxyl group.

Under the influence of 50% sulfuric acid the vinylethynylcarbinol (II) loses water to give the butoxydienyne (IV), which is readily hydrated in aqueous methanol solution to the corresponding butoxy ketone (X).

The hydrogenation products of the above enumerated unsaturated compounds were prepared and described.

LITERATURE CITED

[1] S. A. Vartanyan and V. N. Zhamagortsyan, J. Gen. Chem., Suppl. II, 963 (1953).

[2] I. N. Nazarov and V. M. Romanov, Bull. Acad. Sci. U.S.S.R., Div. Chem. Sci., 453 (1940); I. N. Nazarov and V. M. Romanov, Bull. Acad. Sci. U.S.S.R., Div. Chem. Sci., 559 (1940).

[3] M. H. Palomaa, Chem. Zentr., II, 966 (1912)I.N. Nazarov and V. M. Romanov, Bull. Acad. Sci. U.S.S.R., Div. Chem. Sci., (1940), 453.

[4] I. N. Nazarov and I. I. Zaretskaya, Bull. Acad. Sci. U.S.S.R., Div. Chem. Sci., (1942), 200; (1941), 210.

[5] Chem. Zentr. II, 756 (1950).

Received May 31, 1954.

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SYNTHESIS AND CATALYTIC HYDROGENATION OF THE ACETATE OF 2,7-DIMETHYLOCTA-3,5-DIYN-2,7-DIOL

A. I. Nogaideli and G. M. Gonadze

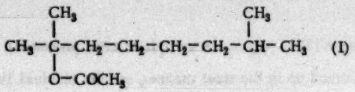
Yu. S. Zalkind with coworkers synthesized a number of acetylene γ-glycol esters with the aid of acetic anhydride and studied the character of their catalytic hydrogenation [1].

Up to now the esters of diacetylene glycols have been studied only slightly. We decided to synthesize the acetate of 2,7-dimethylocta-3,5-diyn-2,7-diol and study its catalytic hydrogenation.

Treatment of 2,7-dimethylocta-3,5-diyn-2,7-diol with acetic anhydride gave the diacetate in 60% yield, appearing as a slightly yellow liquid with b.p. 148-151° at 4 mm, m.p. 31-32°.

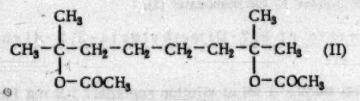
The ester was hydrogenated in the presence of Pt black and of colloidal Pd. It was revealed that in the presence of Pt black the ester vigorously adds hydrogen with a gradual decrease in the hydrogenation rate, in which connection the absorption of hydrogen continues even after 8 atoms of hydrogen have been added. If the reaction is terminated after the addition of the theoretical amount of hydrogen (8 atoms), then, on working up the hydrogenation product a clear, mobile liquid with an aromatic odor is obtained, the fractional distillation of which gave two substances with b.p. 72-74° (I) and 106-108° (II) at 4-5 mm.

Analysis revealed that (I) is the saturated monoester (yield 22.5%).



(I)

Compound (II) proved to be the saturated diester (main product):



(II)

The diacetylene ester in the presence of Pt black is capable of adding a total of 10 atoms of hydrogen with the formation of only the saturated monoester (I).

In the presence of colloidal Pd the diacetylene ester is more vigorously hydrogenated than in the presence of Pt, and in this case the ester adds more than 8 atoms of hydrogen. The hydrogenation results are analogous to those obtained on Pt.

In the presence of colloidal Pd the diacetylene glycol 2,7-dimethylocta-3,5-diyn-2,7-diol is hydrogenated at a slower rate than the corresponding diacetylene ester.

EXPERIMENTAL

Synthesis of the Acetate of 2,7-Dimethylocta-3,5-diyn-2,7-diol

A mixture of 10 g of the diacetylene glycol with m.p. 130-131°, 50 g of acetic anhydride and 1.3 g of anhydrous sodium acetate was heated in an oil bath for 5 hours under reflux at 155-165°. After cooling, the mixture was diluted with water, neutralized with soda, the water layer was separated and extracted with ether. The ether extract was added to the oil layer. After drying over sodium sulfate and removing the ether by distillation, there remained a fairly viscous brownish liquid, which distilled at 148-151° at 4 mm. The oil crystallized and had m.p. 31-32° (from alcohol).

d_{20}^{20} 1.0380, n_D^{20} 1.4908.

0.1030 g substance: 0.2526 g CO_2; 0.0732 g H_2O. 0.0108 g substance; 0.10 g camphor: Δt 17°.

Found %: C 66.90; H 7.89. M 254. $C_{14}H_{18}O_4$. Calculated %: C 67.20; H 7.20; M 250.

The Chugaev-Tserevitinov reaction for active hydrogen is negative. Saponification of the ester gives the original diacetylene glycol with m.p. 130-131°.

Hydrogenation of the Acetate of 2,7-Dimethylocta-3,5-diyn-2,7-diol in the Presence of Pt Black.

2.50 g of ester (0.01 mole), 50 ml of ethanol, 0.75 g of Pt black; 742 mm, 16°, $4H_2$ 971 ml. The amount (in ml) of hydrogen absorbed every 10 minutes was: 180, 173, 165, 162, 165, 133; a total of 978 ml in 60 minutes.

The hydrogenation product was worked up and two substances were isolated from the residual liquid: (I) with b.p. 72-74° at 4 mm (22.5% yield), and (II) with b.p. 106-108° at 4 mm (main product). Both fractions were clear, mobile liquids with an aromatic odor.

Analysis of substance with b.p. 72-74° (4 mm) (I)
d_4^{20} 0.8658, n_D^{20} 1.4250, MR_D 59.08; calculated 59.27.
0.0746 g substance: 0.1966 g CO_2; 0.07820 g H_2O. 0.0434 g substance; 15.65 g benzene: Δt 0.07°. 0.5236 g substance: 5.19 ml 0.5 N KOH. Found %: C 71.87; H 11.64; CH_3CO 21.31. M 201.9. $C_{12}H_{24}O_2$. Calculated %: C 72.00; H 12.00; CH_3CO 21.48. M 200.

The reaction for active hydrogen was negative. The Bukhovits test for triple bond was negative.

Analysis of substance with b.p. 106-108° (4 mm) (II)
d_4^{20} 0.9736, n_D^{20} 1.4430, MR_D 70.45; calculated 70.16.
0.0976 g substance: 0.2231 g CO_2; 0.0890 g H_2O. 0.0684 g substance; 14.64 g benzene: Δt 0.092°. 0.0726 g subs: 5.60 ml 0.1 N KOH. Found %: C 65.14; H 10.13; $2CH_3CO$ 33.21. M 258.9. $C_{14}H_{26}O_4$. Calculated %: C 65.11; H 10.03; $2CH_3CO$ 33.33. M 258.

The Chugaev-Tserevitinov reaction for hydroxyl group was negative. The reaction for triple bond was negative.

The addition of 5 moles of hydrogen (1226 ml) to the acetylene ester proceeded under similar conditions.

The hydrogenation product was worked up in the usual manner, and the residual liquid almost completely distilled in the range 72-74° at 4-5 mm.

From its constants the liquid corresponded to the monoester (I).

Hydrogenation of the Acetate of 2,7-Dimethylocta-3,5-diyn-2,7-diol in the Presence of Colloidal Pd.

Colloidal Pd was prepared on wheat starch: 1 ml of solution contained 1.8 mg Pd. The activity of the catalyst was verified on 2,7-dimethylocta-3,5-diyn-2,7-diol. For 1.66 g of this glycol the hydrogenation reaction to saturation took 168 minutes.

2.5 g of the diacetylene ester (0.012 mole), 50 ml of ethanol, 18 mg of Pd, 732 mm, 15°, $4H_2$ 980 ml.

The amount of hydrogen absorbed every 3 minutes was (in ml.): 225, 145, 155, 75, 80, 75, 45, 50, 37, 23, 25, 20, 10, 7.7; a total of 979 ml for 45 minutes.

After suitable treatment the product was distilled in vacuo. The yield of monoester was 20 %, the main product was the diester.

SUMMARY

1. The acetate of 2,7-dimethylocta-3,5-diyn-2,7-diol was synthesized and described for the first time. The catalytic hydrogenation of the indicated ester was studied in the presence of Pt black and of colloidal Pd. It was shown that in both cases when 8 atoms of hydrogen are absorbed the hydrogenation product is a mixture of the saturated mono- and saturated diester; in this connection the diacetylene ester is capable of adding a total of 5 moles of hydrogen with the formation of only the saturated monoester.

2. The diacetylene ester is more rapidly hydrogenated than the corresponding diacetylene glycol.

The nonselectivity of the hydrogenation process is sharply expressed.

3. Described for the first time in this work are: the acetate of 2,7-dimethyl-2-octanol and the diacetate of 2,7-dimethyl-2,7-octanediol.

LITERATURE CITED

[1] Yu. S. Zalkind and I. G. Bessonova, J Russ. Chem. Soc., 53, 286 (1921); Yu. S. Zalkind and Z. Neishtab, J. Russ. Chem. Soc., 50, 34 (1918); Yu. S. Zalkind and P. S. Bataev, J. Gen. Chem., 17, 1858 (1947); Yu. S. Zalkind and I. M. Gverdtsiteli, J. Gen. Chem., 9, 855 (1939); A. I. Nogaideli and K. Ya. Dzagnidze, J. Gen. Chem., 11, 136 (1941).

Received May 25, 1954.

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CONDENSATION OF DIMETHYLVINYLCARBINOL WITH PHENOL IN THE PRESENCE OF PHOSPHORIC ACID AND ASKANITE

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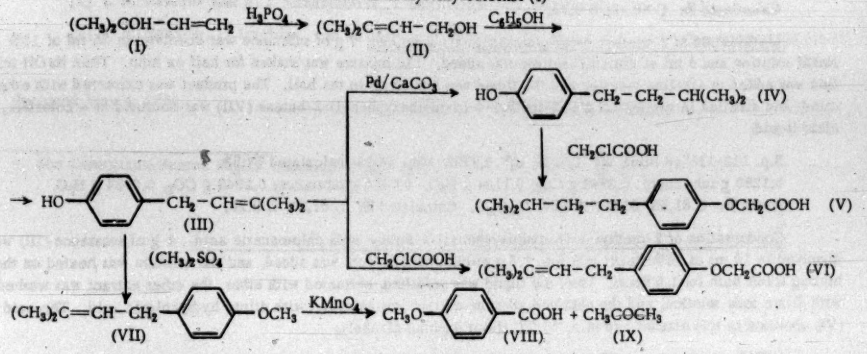
The condensation of phenol with 5-methyl-1,3-hexadien-5-ol in the presence of phosphoric acid was realized by Nazarov and Kakhniashvili [1]. It was shown that the condensation of phenol with a tertiary diene alcohol is accompanied by diene isomerization.

The condensation of dialkylvinylcarbinols with phenols in the presence of phosphoric acid and askanite has not been studied up to now.

To study this condensation we selected dimethylvinylcarbinol (I)



The condensation of dimethylvinylcarbinol (I) with phenol in the presence of phosphoric acid or askanite (clay, activated with sulfuric acid) is accompanied by isomerization of the tertiary carbinol (I) into the primary alcohol – γ,γ-dimethylallyl alcohol (II) and the formation of the para-substituted phenol (III) from it.

We were unable to establish the presence of the corresponding para-substituted phenol in the condensation produ from phenol with dimethylvinylcarbinol.

When hydrogenated with Pd on calcium carbonate the para-substituted phenol absorbs the theoretical amount for 1 mole of hydrogen and is converted into 2-methyl-4-hydroxyphenylbutane (IV).

Methylation of the para-substituted phenol (III) with dimethyl sulfate gives the methyl ether (VII), which on oxidation gives anisic acid (VIII) and acetone (IX). The reaction of the para-substituted phenols (III) and (IV) with chloroacetic acid gave the corresponding crystalline derivatives: 2-methyl-4-(p-carboxymethoxyphenyl)-2-butene (VI) and 2-methyl-4-(p-carboxymethoxyphenyl)butane (V) [4-(2-methyl-2-butenyl)phenoxyacetic acid (VI) and 4-(2-methylbutyl)phenoxyacetic acid (V)].

EXPERIMENTAL

Dimethylvinylcarbinol was prepared by the hydrogenation of dimethylethinylcarbinol with the aid of Pd on calcium carbonate.

B. p. 95-96°, n_D^{20} 1.414 [2].

Condensation of dimethylvinylcarbinol with phenol in the presence of phosphoric acid. To a mixture of 10 g of phenol and 8 ml of phosphoric acid (d 1.704) was added dropwise 11 g of dimethylvinylcarbinol at room temperature and with constant stirring. The reaction is exothermic and the temperature of the mixture at the end of carbinol additio

reaches 45°. After all of the carbinol has been added the mixture is stirred for another hour. The reaction mass is diluted with ether, washed with water, and then washed several times with 10% NaOH solution.

The alkaline extracts are combined, acidified with dilute hydrochloric acid, extracted with ether, the ether extract is dried over sodium sulfate and, after removal of the ether, is vacuum distilled.

Vacuum distillation of the product gave 6 g of 2-methyl-4-(p-hydroxyphenyl)-2-butene (III):

B.p. 127-128° (7 mm), n_D^{20} 1.5345, d_4^{20} 0.9966, MR_D 50.56; calculated 50.54.
0.0832 g substance; 0.2492 g CO_2; 0.0652 g H_2O. Found %: C 81.70; H 8.84. $C_{11}H_{14}O$.
Calculated %: C 81.48; H 8.64.

Hydrogenation of 2-methyl-4-(p-hydroxyphenyl)-2-butene. 700 ml of hydrogen (19°, 729 mm) was absorbed when 5 g of the substance in 25 ml of ethyl alcohol was hydrogenated in the presence of 0.3 g of Pd on calcium carbonate (theory 700 ml). The catalyst was filtered, the alcohol was removed by distillation, and the product was distilled. The yield of 2-methyl-4-(p-hydroxyphenyl)butane (IV) was 3.5 g.

B.p. 128-130° (7 mm), n_D^{20} 1.5165, d_4^{20} 0.9665.
0.0626 g substance: 0.1844 g CO_2; 0.0560 g H_2O. Found %: C 80.74; H 9.90. $C_{11}H_{16}O$.
Calculated %: C 80.48; H 9.75.

Methylation of 2-methyl-4-(p-hydroxyphenyl)-2-butene. 7 g of substance was dissolved in 35 ml of 10% NaOH solution and 6 ml of dimethyl sulfate was added. The mixture was shaken for half an hour. Then NaOH solution was added to alkaline reaction and the liquid was heated up to the boil. The product was extracted with ether, dried, and distilled in vacuo; 3.2 g of 2-methyl-4-(p-methoxyphenyl)-2-butene (VII) was obtained as a colorless, clear liquid:

B.p. 113-115° (6 mm), n_D^{20} 1.5238, d_4^{20} 0.9793, MR_D 54.79; calculated 54.83.
0.1280 g substance: 0.3843 g CO_2; 0.1134 g H_2O. 0.0984 g substance: 0.2942 g CO_2; 0.0824 g H_2O.
Found %: C 81.50, 81.36; H 9.24. $C_{12}H_{16}O$. Calculated %: C 81.81; H 9.20.

Condensation of 2-methyl-4-(p-hydroxyphenyl)-2-butene with chloroacetic acid. 1 g of substance (III) was dissolved in 10 ml of 10% NaOH solution, 1.5 g of chloroacetic acid was added, and the mixture was heated on the boiling water bath for 1.5 hours. Then the liquid was acidified, extracted with ether, the ether extract was washed with dilute soda solution, and the obtained alkaline extract was acidified with dilute hydrochloric acid. The acid (VI) obtained in this manner had m.p. 76-77° (from aqueous alcohol).

0.0708 g substance: 0.1841 g CO_2; 0.0460 g H_2O. 0.1053 g substance: 4.6 ml 0.1 N NaOH.
Found %: C 70.90; H 7.07. M 228.2. $C_{13}H_{16}O_3$. Calculated %: C 70.90; H 7.27. M 220.

The analytical data correspond to 2-methyl-4-(p-carboxymethoxyphenyl)-2-butene (VI).

Oxidation of 2-methyl-4-(p-methoxyphenyl)-2-butene. 2.5 g of substance (VII) was added to a solution of 0.5 g of potash in 100 ml of water; to the obtained mixture with stirring and cooling was added 7 g of finely ground potassium permanganate. The manganese dioxide was filtered and washed several times with hot water. The 200 ml of combined solution was distilled to remove 120 ml of water together with volatile neutral products. The distillate was saturated with potash and again 40 ml of liquid was removed by distillation. Treatment of the distillate with an aqueous solution of iodine and sodium hydroxide gave a copious precipitate of iodoform and a red color with sodium nitroprusside (acetone).

After removal of the neutral products by distillation, the residue was evaporated to small volume and acidified with hydrochloric acid; the crystals obtained in this manner had m.p. 180-182° (from water). The mixed melting point with p-methoxybenzoic acid failed to give a depression.

Condensation of dimethylvinylcarbinol with phenol in the presence of askanite was carried out under the same conditions as in the presence of phosphoric acid, the only difference being that the stirring at room temperature was continued for 5 hours, after which the mixture was stirred at 40-45° for 10 hours. 3.5 g of 2-methyl-4-(p-hydroxyphenyl)-2-butene was obtained.

Condensation of 2-methyl-4-(p-hydroxyphenyl)butane (IV) with chloroacetic acid was carried out under the same conditions as in the condensation of (III); the obtained acid (V) had m.p. 103-104° (from aqueous alcohol).

0.1456 g substance; 0.3746 g CO_2; 0.1056 g H_2O. 0.0821 g substance; 3.8 ml 0.1 N NaOH.
Found %: C 70.16; H 8.03. M 216. $C_{13}H_{18}O_3$. Calculated %: C 70.27; H 8.10. M 222.

The analytical data correspond to 2-methyl-4-(p-carboxymethoxyphenyl)butane (V).

SUMMARY

1. In the condensation of phenol with dimethylvinylcarbinol in the presence of phosphoric acid or askanite the first reactionobserved is the allyl rearrangement of dimethylvinylcarbinol into γ,γ-dimethylallyl alcohol and the formation of 2-methyl-4-(p-hydroxyphenyl)-2-butene.

2. The methylation of 2-methyl-4-(p-hydroxyphenyl)-2-butene with dimethyl sulfate gave 2-methyl-4-(p-methoxyphenyl)-2-butene, the oxidation of which gave anisic acid and acetone.

3. In the hydrogenation of 2-methyl-4-(p-hydroxyphenyl)-2-butene 1 mole of hydrogen is absorbed to give 2-methyl-4-(p-hydroxyphenyl)butane.

4. The condensation of 2-methyl-4-(p-hydroxyphenyl)-2-butene with chloroacetic acid gave 2-methyl-4-(p-carboxymethoxyphenyl)-2-butene, while the condensation of chloroacetic acid with 2-methyl-4-(p-hydroxyphenyl)butane gave 2-methyl-4-(p-carboxymethoxyphenyl)butane.

LITERATURE CITED

[1] I. N. Nazarov and A. I. Kakhniashvili, J. Gen. Chem., 22, 617 (1952). *

[2] I. N. Nazarov, I. Azerbaev, and V. Rakcheeva, Bull. Acad. Sci. U.S.S.R., Div. Chem. Sci., 392 (1942).

Received May 4, 1954.

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* See Consultants Bureau English translation, page 677.

REACTION OF BIS-β-HYDROXYETHYLANILINE AND BIS-β-HYDROXYPROPYLANILINE WITH FORMALDEHYDE

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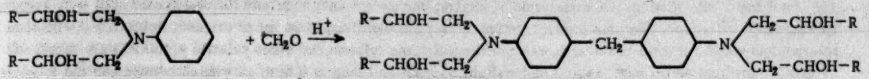
For further study of the reaction between aromatic amino alcohols and aldehydes [1-5], we investigated the reaction of bis-β-hydroxyethylaniline and bis-β-hydroxypropylaniline with formaldehyde; on doing this it was established that the indicated alkanolanilines react with formaldehyde to give the corresponding amino alcohols (I-II) of the diaminodiphenylmethane series.



where R = H (I) and CH_3 (II)

We used hydrochloric and formic acids as catalyst in this reaction. The amino alcohols (I, II) were obtained in a yield of 90-93%. The structure of p,p'-tetra-β-hydroxyethyldiaminodiphenylmethane (I) and of p,p'-tetra-β-hydroxypropyldiaminodiphenylmethane (II) is conditioned by the scheme of their formation, the acceptance of which does not contradict the generally accepted principles relative to the reactions of N-alkylanilines with aldehydes, which, as is known, proceed at the para-position [6, 7]. Consequently, the condensation of formaldehyde with bis-β-hydroxyethylaniline and bis-β-hydroxypropylaniline, having in their composition the atom grouping $-CH_2-N-CH_2-$, which is structurally close to the dialkylanilines, also undoubtedly proceeds at the para-position. This also agrees with our earlier observations made on the condensation of N-aryloxazolidines with formaldehyde [5].

In addition to the amino alcohols (I, II), we also obtained the tetra-acetate of p,p'-tetra-β-hydroxyethyldiaminodiphenylmethane in the present study.

EXPERIMENTAL

1. p,p'-Tetra-β-hydroxyethyldiaminodiphenylmethane (I) (p,p'-tetraethanoldiaminodiphenylmethane). Into a 1 liter round-bottomed flask, fitted with stirrer and reflux condenser, was introduced 181 g (1 mole) of bis-β-hydroxyethylaniline (diethanolaniline), dissolved in 600 ml of 25% alcohol, 45 ml (0.55 mole) of 36% formalin, and 2 ml of hydrochloric acid (d. 1.18). The reaction was run at 30-35° for 40 hours and was accompanied by the formation of a white crystalline precipitate, the separation of which began 6 hours after the start of the reaction. On completion of the process the reaction mass was cooled to room temperature and neutralized with soda solution. The crystals were suction filtered on a Nutsch filter, washed with water, then with a small amount of alcohol, and finally air dried. The yield of crystals was 165 g or 91%. The obtained product had an m.p. of 114-115°. p,p'-tetraethanoldiaminodiphenylmethane is readily soluble in alcohol and benzene. Recrystallization from 50% alcohol gave white needles with an m.p. of 117.5°, which, with time, turned blue in the air.

0.3771 g substance: 19.6 ml 0.1 N H_2SO_4. 0.2818 g substance: 14.85 ml 0.1 N H_2SO_4. 0.3376 g substance: 7.05 ml 0.5 N KOH. 0.3563 g substance: 7.25 ml 0.5 N KOH. Found %: N 7.27, 7.37; OH 17.74, 17.29. $C_{21}H_{28}O_4N_2$. Calculated %: N 7.48; OH 18.18

In addition, p,p'-tetra-β-hydroxyethyldiaminodiphenylmethane was prepared using 5 ml of 85% formic acid (per mole of starting diethanolaniline) as the catalyst. In this case the reaction was run without heating and was accompanied by a slight evolution of heat; the yield of product in this case was 93%.

2. p,p'-Tetra-β-hydroxypropyldiaminodiphenylmethane (II). A mixture of 209 g (1 mole) of bis-β-hydroxypropylaniline and 45 ml (0.55 mole) of 36% formalin in 400 ml of 50% alcohol was heated on the water bath at 80-90° in the presence of 2 ml of hydrochloric acid (d. 1.18) for 25 hours with constant stirring. The obtained product settled on the bottom of the flask as a heavy oil. The product was diluted with 150 ml of benzene, after which it was neutralized with soda solution and washed with water. The p,p'-tetra-β-hydroxypropyldiaminodiphenylmethane was freed from benzene and impurities by vacuum distillation, in which connection an oil bath was used for the removal of the impurities, at first under slight vacuum and then at 4 mm; the temperature of the oil bath toward the end of the distillation was raised to 200°. After removal of the impurities by distillation

the p,p'-tetra-β-hydroxypropyldiaminodiphenylmethane was obtained as a brown viscous oil, which congealed on standing into a brittle mass that resembled rosin. The yield was 195 g (90.5%).

0.2432 g substance: 11.5 ml 0.1 N H_2SO_4. 0.2327 g substance: 3.6 ml 0.5 N KOH. Found %: N 6.61; OH 15.3. $C_{25}H_{40}O_4N_2$. Calculated %: N 6.48; OH 15.81.

p,p'-Tetra-β-hydroxypropyldiaminodiphenylmethane is readily soluble in the alcohols, and only slightly soluble in hydrocarbon solvents. Recrystallization from benzene gave fine, white crystals with an m.p. of 155-157°.

0.0788 g substance: 3.6 ml 0.1 N H_2SO_4. Found %: N 6.45. $C_{25}H_{40}O_4N_2$. Calculated %: N 6.48.

3. Tetraacetate of p,p'-tetra-β-hydroxyethyldiaminodiphenylmethane (tetraacetate of p,p'-tetraethanoldiaminodiphenylmethane). The tetraacetate of p,p'-tetraethanoldiaminodiphenylmethane was obtained by reacting 47.2 g (0.125 mole) of p,p'-tetraethanoldiaminodiphenylmethane with 77 g (0.125 mole) of p,p'-tetraethanoldiaminodiphenylmethane with 77 g (0.75 mole) of acetic anhydride. The reaction was run in an oil bath at 140-150° for 6 hours with stirring. On conclusion of heating, the excess anhydride and formed acetic acid were removed by vacuum distillation. Then the product (tetraacetate) was dissolved in 90 ml of toluene, neutralized with soda solution and washed several times with water, after which the toluene and other volatile products were removed by distillation from an oil bath, at first under slight vacuum and then at 5 mm, in which connection the temperature of the oil bath toward the end of the distillation was raised to 200°. The residue in the flask (tetraacetate) was not subjected to distillation. After several days this residue congealed into a solid gray crystalline mass, soluble in alcohol and benzene. The yield was 50 g (79%). Recrystallization from 70% alcohol gave the tetraacetate as silvery plates with m.p. 51.5-52.5°.

0.4612 g substance: 16.9 ml 0.1 N H_2SO_4. 0.4605 g substance: 15.9 ml 0.1 N/ H_2SO_4. Found %: N 5.12, 4.84. $C_{29}H_{32}O_8N_2$. Calculated %: N 5.17.

SUMMARY

1. In this study it was shown that the condensation of bis-β-hydroxyethylaniline and bis-β-hydroxypropylaniline with formaldehyde proceeds with the formation respectively of tetra-β-hydroxyethyldiaminodiphenylmethane and tetra-β-hydroxypropyldiaminodiphenylmethane.

LITERATURE CITED

[1] K. D. Petrov, J. Gen. Chem., Suppl. I, 374 (1953).

[2] K. D. Petrov and O. K. Gosteva, J. Gen. Chem., Suppl. II, 1352 (1953).

[3] K. D. Petrov and E. S. Lagucheva, J. Gen. Chem., 23, 403 (1953). •

[4] K. D. Petrov, E. S. Lagucheva, and V. I. Pukhova, J. Gen. Chem., 23, 1771 (1953). ••

[5] K. D. Petrov and O. K. Gosteva, J. Gen. Chem., 23, 1940 (1953). •••

[6] J. Pinnow, Ber., 27, 3166 (1894); J. Houben, Methods of Organic Chemistry, Vol. IV, p. 776 (1949).

[7] P. P. Shorygin, Organic Chemistry, pp. 353, 417 (1940).

Received April 26, 1954.

Scientific Research Institute
for Plastics

• See Consultants Bureau English translation, page 411

•• See Consultants Bureau English translation, page 1869

••• See Consultants Bureau English translation, page 2055

THE CLEAVAGE OF TRIPHENYLANTIMONY WITH ACID CHLORIDES IN THE PRESENCE OF ALUMINUM CHLORIDE

M. S. Malinovsky and S. P. Olifirenko

In 1935, in attempting to run the Friedel-Crafts reaction between phenyldichloroarsine, diphenylchloroarsine, diphenylcyanoarsine and acetyl chloride, it was established by one of us that in all of the investigated reactions there occurs cleavage of the phenyl groups from arsenic, resulting in the formation of acetophenone [1]. Further studies in this field [2, 3] revealed that other acid chlorides also act on the above indicated arsines in a similar manner, i.e., the benzene ring is cleaved from the arsenic. Later, it was established that tetraphenyl lead, tetraphenyl tin and diphenylmercury with acetyl chloride in the presence of aluminum chloride, partially cleave the phenyl groups in the form of acetophenone [4]. Analogous studies on compounds of lead, tin and mercury were made by Kocheshkov and Skoldinov [5]. Finally, in 1948 Dolgov and Panina described the behavior of triethylphenylmonosilane under the conditions of the Friedel-Crafts reaction. The authors mention the formation of organic ketones with benzene being formed as a by-product [6].

On the basis of the above presented studies we came to the conclusion that in the presence of aluminum chloride the acid chlorides will also act in a similar manner on many other organometallic compounds with aromatic radicals, and specifically, on antimony compounds.

To support this postulation, we made the present study, using as the acid chlorides, the compounds acetyl, propionyl, isobutyryl, isovaleryl, and benzoyl chlorides. The obtained results confirmed our theory: triphenylantimony is cleaved at the antimony-phenyl bond independent of the acid chloride used, with the resultant formation of the corresponding ketones.

On the basis of the above the general reaction for the decomposition of triphenylantimony can be written in the form:

$$(C_6H_5)_3Sb + 3Cl-CO-R \xrightarrow{AlCl_3} 3C_6H_5COR + SbCl_3.$$

The presence of antimony trichloride was confirmed by the fact that after the reaction products were decomposed with water the treatment of the aqueous solution with hydrogen sulfide gave a precipitate of antimony trisulfide.

In addition to the ketones, we isolated phenyldichloroantimony from the reaction products. However, in not a single instance were we able to establish the formation of benzene, a product that was found to be present in the analogous cleavage of triethylphenylsilicon [6]. Also, we failed to isolate any unchanged stibine.

The presence of phenyldichloroantimony indicates the stepwise character of the reaction, in which the formation of the intermediate organoaluminum compound is possible [5]. To confirm the latter we studied the relation of triphenylantimony to aluminum chloride. It was revealed that we were unable to isolate any unchanged stibine even when aluminum chloride alone was allowed to act on triphenylantimony. In the reaction products we found $C_6H_5SbCl_2$, $C_6H_5SbOCl_2$ and antimony trichloride (confirmed by the formation of antimony sulfide from hydrogen sulfide), and also benzene.

The obtained results make it possible to postulate the following mechanism for the decomposition of triphenylantimony:

$$(C_6H_5)_3Sb + AlCl_3 \longrightarrow (C_6H_5)_2SbCl + C_6H_5AlCl_2 \quad (1)$$

$$(C_6H_5)_2SbCl + AlCl_3 \longrightarrow C_6H_5SbCl_2 + C_6H_5AlCl_2 \quad (2)$$

$$C_6H_5SbCl_2 + AlCl_3 \longrightarrow SbCl_3 + C_6H_5AlCl_2. \quad (3)$$

The formation of benzene in the case of conducting the reaction in the absence of acid chlorides is the result of the action of water on the organoaluminum compound:

$$C_6H_5AlCl_2 + 3H_2O \longrightarrow C_6H_6 + 2HCl + Al(OH)_3. \quad (4)$$

However, if an acid chloride is present in the reaction mixture, then the latter reacts with the organoaluminum compound, forming a ketone in accord with the equation:

$$C_6H_5AlCl_2 + Cl-CO-R \longrightarrow C_6H_5-CO-R + AlCl_3. \quad (5)$$

In conclusion, we wish to mention that in all of the experiments a considerable amount of tar is formed, this tar containing from 9 to 18 % antimony.

EXPERIMENTAL

Cleavage of triphenylantimony with acid chlorides in the presence of aluminum chloride. For the experiments were taken 17.68 g (0.05 mole) of triphenylantimony, 0.15 mole of acid chloride, 20 g of aluminum chloride, and 75 g of carbon disulfide.

The triphenylantimony was placed in a three-necked flask, which was fitted with a dropping funnel, reflux condenser (the top of which was closed with a calcium chloride tube) and stirrer. The carbon disulfide was poured into the flask and the stibine was added, after the solution of which the aluminum chloride was added. Then, with ice cooling of the flask, and stirring, the acid chloride was added dropwise over a period of 1.5 hours. In approximately 20 minutes after the beginning of acid chloride addition the contents of the flask begin to separate into two layers. On conclusion of reaction the mixture was allowed to stand overnight, after which it was heated on the water bath for 2 hours (at 50-80°), and then after cooling it was cautiously decomposed with ice water. The carbon disulfide layer was separated and dried over calcium chloride, while the water layer was extracted with ether and the ether layer also dried over calcium chloride. To the residue after the removal of carbon disulfide by distillation, was added the ether extract, and the ether was removed by distillation. The residue was distilled in vacuo.

The ketone was isolated from the lower boiling fractions, after which it was again redistilled in a narrow temperature range.

The physical constants for the ketone were determined and the semicarbazone was prepared. The data on the ketones is given in the table.

Ketones Obtained from Triphenylstibine

Acid chloride used in the reaction	Obtained ketone	Yield (in g)	B.p. of ketone	n_D^{20}	d_4^{20}	M.p. of semicarbazone	Literature references
Acetyl chloride	$C_6H_5COCH_3$	9	200 - 202°	1.532	1.030	197 - 198°	[7]
Propionyl chloride	$C_6H_5COC_2H_5$	12	218	1.526	1.013	173	[8]
Isobutyryl chloride	$C_6H_5COC_3H_7$-iso	14	219 - 221	1.517	0.9899	166	[8]
Isovaleryl chloride	$C_6H_5COC_4H_9$-iso	14	230 - 231	1.504	0.9710	208	[8]
Benzoyl chloride	$C_6H_5COC_6H_5$	4.1	M.p. 48	–	–	–	[7]

The fraction, boiling in the range of 100-115° at 10 mm, rapidly congealed into crystals with m.p. 62° (from ether). The amount of antimony and chlorine in this fraction corresponds to the formula $C_6H_5SbCl_2$.

Found %: Sb 44.95; Cl 26.20. $C_6H_5SbCl_2$. Calculated %: Sb 45.15; Cl 26.29.

Treatment of the aqueous solution (after decomposition of the flask contents with ice water) with hydrogen sulfide gave a precipitate of antimony sulfide, which was analyzed.

Found %: Sb 71.32; S 28.25. Sb_2S_3. Calculated %: Sb 71.68; S 28.32.

Action of aluminum chloride on triphenylantimony. The experiment was repeated without the addition of an acid chloride. The reaction mixture was worked up as before. From the reaction products were obtained 2 g of benzene, b.p. 80°, d_4^{20} 0.882, n_D^{20} 1.501; the nitration of this fraction gave nitrobenzene. In addition to benzene there were obtained: 3.1 g of $C_6H_5SbCl_2$ with m.p. 62°, verified by analyzing it for antimony and chlorine, and 6.5 g of $C_6H_5SbOCl_2$, confirmed by analysis.

Found %: Sb 42.03; Cl 24.05. $C_6H_5SbOCl_2$. Calculated %: Sb 42.62; Cl 24.82.

1.6 g of antimony sulfide was obtained from the aqueous solution. The residue (5.3 g) in the flask was tar, containing 11.02% antimony.

SUMMARY

1. Triphenylantimony in the presence of anhydrous aluminum chloride does not undergo the Friedel-Crafts reaction with acid chlorides, but instead cleaves at the C_6H_5-Sb bond.

2. With the five investigated acid chlorides, triphenylantimony in the presence of aluminum chloride formed the corresponding ketones.

3. A mechanism is proposed for the cleavage of triphenylantimony by acid chlorides in the presence of aluminum chloride, based on the assumption that an organoaluminum compound is formed as an intermediate product.

LITERATURE CITED

[1] M. Malinovsky, J. Gen. Chem., 5, 1355 (1935).

[2] M. Malinovsky, Sci. Reports Gorky State Univ., No. 7, 34 (1936).

[3] M. Malinovsky, J. Gen. Chem., 19, 130 (1949). *

[4] M. Malinovsky, Trans. Gorky State Pedagogy Inst., 5, 39 (1940).

[5] K. Kocheshkov and A. Skoldinov, J. Gen. Chem., 12, 398 (1942).

[6] B. Dolgov and O. Panina, J. Gen. Chem., 18, 1291 (1948).

[7] G. Clark, Manual of Qualitative and Quantitative Organic Analysis (1934).

[8] K. Auwers, Ber., 45, 2771 (1912).

Received May 7, 1954.

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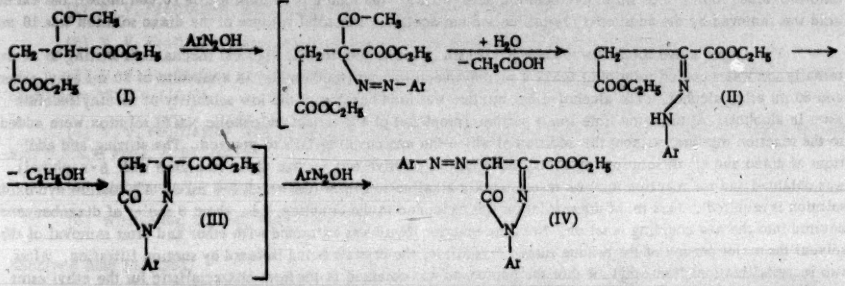
* See Consultants Bureau English translation, page 119

THE ACTION OF AROMATIC DIAZO COMPOUND ON ALKYLACETOACETIC ESTERS AS A METHOD FOR THE PREPARATION OF ARYLHYDRAZONES OF KETO ACIDS, α-AMINO ACIDS, AND NITROGEN HETEROCYCLIC COMPOUNDS

XVII. THE REACTION OF SUCCINYLSUCCINIC ESTER WITH AROMATIC DIAZO COMPOUNDS

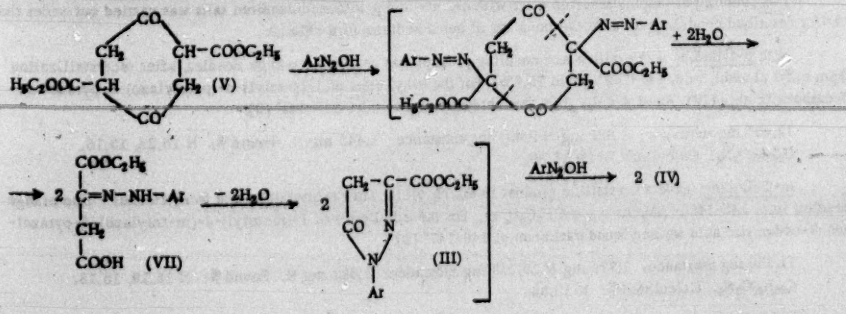
V. V. Feofilaktov and T. N. Ivanova

In previous papers one of us [1, 2] studied the azo coupling of acetosuccinic ester (I) with aryl diazonium compounds for the purpose of obtaining arylhydrazones of oxalacetic acid. However, instead of the expected arylhydrazones (II), we obtained derivatives of pyrazolone – the ethyl esters of 1-aryl-4-arylazo-5-pyrazolone-3-carboxylic acid (IV) – as the main product. As can be assumed, the arylhydrazones of the ethyl ester of oxalacetic acid (II) formed in the first stage of the reaction, under the reaction conditions are so quickly cyclized into pyrazolones (III), and the latter in their turn so readily enter again into the azo coupling reaction (III → IV), that this reaction cannot as yet be used for the preparation of the indicated arylhydrazones, but because of this great reactivity it proved to be a convenient general method for the preparation of the ethyl esters of 1-aryl-4-arylazo-5-pyrazolone-3-carboxylic acid (IV), i.e., tartrazine and its analogs, obtained in one reaction step and with high yields [2, 3].



In the present communication, we present the results of attempting to prepare the arylhydrazones of oxalacetic acid by using succinylsuccinic ester (V) in the azo coupling reaction, for which ability both for azo coupling and for undergoing hydrolytic cleavage under the azo coupling conditions can be expected, by analogy, for example, with the behavior of 2-carbethoxycyclohexanone [4] under these conditions.

However, here also, as in the case of acetosuccinic ester, instead of the expected arylhydrazones of the acid ester of oxalacetic acid (VII) the solitary reaction product of azo coupling proved to be the same derivatives of pyrazolone – the ethyl esters of 1-aryl-4-arylazo-5-pyrazolone-3-carboxylic acid (IV). The process for their formation can be depicted by the following scheme:



By analogy with the earlier-studied cases of azo coupling of alkylacetoacetic esters, the initial product is, apparently, the azo ester (VI), which, as the result of hydrolytic cleavage of the ring in 1,4-cyclohexandione, is transformed into the arylhydrazone of the acid ester of oxalacetic acid (VII); the latter under the reaction conditions undergoes cyclization into the pyrazolone derivative, forming the ethyl ester of 1-aryl-5-pyrazolone-3-carboxylic acid (III), the isolation of which is, however, impossible, inasmuch as because of its active methylene group it again couples with the diazo component (III → IV).

The formation of these 4-arylazopyrazolone derivatives is the chief reaction and we were unable to stop the reaction at the intermediate stages, the 4-arylazopyrazolones undoubtedly being formed as the result of azo coupling: in lower yields when insufficient amounts of diazo compound are used (for example, 2 moles of diazo for 1 mole of succinylsuccinic ester), and in yields of 65-85% when up to 4 moles of diazo are added.

The diazo components chosen by us were benzenediazonium and the three toluenediazonium (ortho-, meta- and para-) compounds.

EXPERIMENTAL

The starting succinylsuccinic ester, prepared by the Liebermann method [5], had an m.p. of 126-127°.

Coupling of succinylsuccinic ester with benzenediazonium salt – the preparation of the ethyl ester of 1-phenyl-4-phenylazo-5-pyrazolone-3-carboxylic acid (IV, Ar= C_6H_5)

The solution of benzenediazonium chloride was prepared in the usual manner from 1.04 g of aniline hydrochloride (0.008 mole), 0.88 ml of hydrochloric acid (d 1.19), and 0.56 g of sodium nitrite (0.008 mole); the excess acid was removed by the addition of crystalline sodium acetate. The total volume of the diazo solution was 16 ml.

The cooled diazo solution was gradually added in a fine stream with vigorous mechanical stirring to an externally ice water cooled solution of 0.512 g succinylsuccinic ester (0.002 mole) in a mixture of 30 ml ethyl ether and 50 ml ethyl alcohol. (The alcohol-ether mixture was used because of the low solubility of succinylsuccinic ester in alcohol). At the same time small portions (dropwise) of 4% aqueous-alcoholic NaOH solution were added to the reaction mixture, without the addition of which the azo coupling fails to proceed. The stirring and additions of diazo and alkali solutions were continued until a positive test for free diazo (reaction with β-naphthol) was obtained and the reaction mixture tested weakly alkaline to litmus (for which 5-6 ml of 4% sodium hydroxide solution is required). 11.2 ml of diazo solution was expended in the coupling, i.e., about 3 moles of diazobenzene entered into the azo coupling reaction. Next the reaction liquid was extracted with ether and after removal of the solvent the major portion of the residue turned crystalline, the crystals being isolated by suction filtration. After two recrystallizations from ethyl alcohol the compound was obtained in the form characteristic for the ethyl ester of 1-phenyl-4-phenylazo-5-pyrazolone-3-carboxylic acid, orange, fine needlelike crystals, m.p. 152-153°. Yield 0.88 g (65.5%).

Literature data: m.p. 152-154 [6]; 152-153 [1].
11.410 mg substance: 1.877 mg N_2. 10.180 mg substance: 1.676 mg N_2(Kjeldahl). Found %: N 16.45, 16.41. $C_{18}H_{18}O_3N_4$. Calculated %: N 16.67.

Coupling of succinylsuccinic ester with toluenediazonium salts – the preparation of ethyl esters of 1-tolyl-4-tolylazo-5-pyrazolone-3-carboxylic acid

The coupling of succinylsuccinic ester with o-, m- and p-toluenediazonium salts was carried out under the earlier described conditions used for the coupling of benzenediazonium chloride.

With p-toluidine a crystalline azo coupling product was obtained – orange needles, after recrystallization from ethyl alcohol, m.p. 141-142°, yield 76.9%. For the ethyl ester of 1-(p-tolyl)-4-(p-tolylazo)-5-pyrazolone-3-carboxylic acid (IV), Ar = 1.4-$CH_3C_6H_4$–, we obtained earlier m.p. 143-144° [2].

12.400 mg substance: 1.891 mg N 9.494 mg substance: 1.440 mg N. Found %: N 15.25, 15.16. $C_{20}H_{20}O_3N_4$. Calculated %: N 15.39.

m-Toluidine gave a crystalline product in 85.3% yield, after recrystallization from alcohol – fine orange needles, m.p. 145-146°. (IV, Ar = 1.3-$CH_3C_6H_4$–). For the ethyl ester of 1-(m-tolyl)-4-(m-tolylazo)-5-pyrazolone-3-carboxylic acid we had found earlier m.p. 146-147° [2].

11.656 mg substance: 1.770 mg N 10.270 mg substance: 1.533 mg N. Found %: N 15.19, 15.13. $C_{20}H_{20}O_3N_4$. Calculated %: N 15.39.

o-Toluidine gave the azo coupling product in 65% yield. Its purification was difficult because of amorphous impurities; after recrystallization (4-5 times) from alcohol using activated carbon the product was obtained as reddish-orange plates, m.p. 94-95°. For the ethyl ester of 1-(o-tolyl)-4-(o-tolylazo)-5-pyrazolone-3-carboxylic acid (IV, Ar = 1,2-$CH_3C_6H_4$-) we had found earlier m.p. 95-96° [2].

11.986 mg substance: 1.831 mg N. 10.812 mg substance: 1.658 mg N. Found %: N 15.26, 15.33. $C_{20}H_{20}O_3N_4$. Calculated %: N 15.39.

SUMMARY

It was established that the only products of azo coupling succinylsuccinic ester with arylhydrazones under our conditions are pyrazolone derivatives of the type of ethyl esters of 1-aryl-4-arylazo-5-pyrazolone-3-carboxylic acid.

The formation of these compounds indicates the great ease of hydrolytic cleavage of the succinylsuccinic ester ring under the azo coupling conditions, i.e., in weakly alkaline aqueous-alcohol medium and at low temperatures, a property that makes succinylsuccinic ester resemble 2-carbethoxycyclohexanone in this respect, which also suffers hydrolytic cleavage in the azo coupling process.

It must be assumed that the arylhydrazones of the acid ester of oxalacetic acid are capable of spontaneous cyclization into pyrazolone derivatives, a fact that had been established earlier for the arylhydrazones of the full (neutral) ester of oxalacetic acid [1, 2].

LITERATURE CITED

[1] V. V. Feofilaktov, Bull. Acad. Sci. U.S.S.R., Div. Chem. Sci., 2, 263 (1940).

[2] V. V. Feofilaktov, Bull. Acad. Sci. U.S.S.R., Div. Chem. Sci., 4-5, 521 (1941).

[3] V. V. Feofilaktov and M. S. Kozlova, Patent on the Preparation of Tartrazine and its Analogs, Author's Certificate 388950 (1941).

[4] V. V. Feofilaktov, and N. K. Semenova, "Syntheses of Organic Compounds", Suppl. II. Moscow, Acad. Sci. U.S.S.R. Press, p. 98 (1952).

[5] Liebermann, Ann. 404, 287 (1914).

[6] Wislicenus, Scheidt, Ber., 24, 4212; Beilst., XXV 251.

Received June 17, 1954.

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PREPARATION OF SOME NAPHTHYLPROPIONIC ACIDS

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In the preparation of β-1-(4-methoxynaphthyl) propionic acid Windaus [1] and Ruhemann [2] used 4-methoxy-1-naphthaldehyde as the starting material, from which they went to β-1-(4-methoxynaphthyl) acrylic acid (Windaus with the aid of the Perkin reaction, while Ruhemann used the Claisen reaction). β-1-(4-Methoxynaphthyl) acrylic acid was reduced by means of sodium amalgam; in addition, Ruhemann also used the catalytic hydrogenation method in the presence of colloidal palladium.

We tried a different method for the preparation of β-1-(4-methoxynaphthyl) propionic acid, starting from 1-methoxynaphthalene. 1-Methoxynaphthalene was subjected to chloromethylation, and the 4-methoxy-1-chloromethylnaphthalene thus obtained was condensed with sodiomalonic ester; the product obtained after the condensation was hydrolyzed to 4-methoxynaphthylmalonic acid, which was then decarboxylated:

$$CH_3OC_{10}H_7 \longrightarrow CH_3OC_{10}H_6CH_2Cl \longrightarrow CH_3OC_{10}H_6CH_2CH(COOC_2H_5)_2 \longrightarrow CH_3OC_{10}H_6CH_2CH(COOH)_2 \longrightarrow$$

$$\longrightarrow CH_3OC_{10}H_6CH_2CH_2COOH.$$

None of the substances formed in the intermediate stages were purified, chiefly because of their instability.

The heating of β-1-(4-methoxynaphthyl)propionic acid with hydrobromic acid gave β-1-(4-hydroxynaphthyl) propionic acid, a compound as yet not described in the literature. Attempts to dealkylate the methoxynaphthylpropionic acid by heating it with $AlCl_3$ in benzene solution proved unsuccessful. The methyl and ethyl esters of β-1-(4-hydroxynaphthyl)propionic acid were prepared.

To prepare the β-1-naphthyl- and β-2-naphthylpropionic acids the catalytic hydrogenation of the corresponding naphthylacrylic acids in the presence of Raney nickel was studied; on doing this it was found that because of the difficult solubility of β-1-naphthylacrylic acid in alcohols and the ready solubility of its sodium salt in water, the hydrogenation is most conveniently made in aqueous-alkaline medium, and, in reverse, that the hydrogenation of β-2-naphthylarrylic acid is best made with the free acid in ethyl alcohol solution, inasmuch as the sodium salt of this acid is difficultly soluble in water.

EXPERIMENTAL

β-1-(4-Methoxynaphthyl)propionic Acid

A mixture of 15 g of 1-methoxynaphthalene, 4.8 g of paraform and 180 ml of anhydrous benzene was saturated with HCl gas at 0° with constant stirring; after saturation the benzene solution was filtered, washed with water and dried over potash, after which some of the excess benzene was removed by distillation (in vacuum without heating), and the remaining benzene solution* was gradually added to a previously prepared alcohol solution of sodiomalonic ester (17 g of malonic ester, 50 ml of anhydrous alcohol and 2.1 g of sodium). The additions were made in such a manner as to keep the temperature inside the reaction mixture below 30°; after all the benzene solution had been added, the reaction mixture was allowed to stand overnight at room temperature, and then it was heated for 6 hours. The alcohol was removed by distillation and the residue was treated with water and then extracted with ether. The ether solution was washed with water and dried over sodium sulfate. The ether was removed by distillation, the residue treated with alcoholic KOH solution (10 parts of KOH and 150 ml of anhydrous ethyl alcohol were taken for 22 parts of oily substance), and the mixture heated for 4 hours. On conclusion of heating the alcohol was removed by distillation, the residue was dissolved in water and the alkaline solution was acidified. The precipitated substance has an m.p. of 150-153° (decomp.**). To 2 g of the substance (m.p. 150-153°) obtained in this manner was added 12 ml of pyridine and the solution was heated at around 100° until the evolution of CO_2 ceased. After removal of the pyridine by distillation the residue (1.2 g) was extracted with ether and the substance remaining after removal of the ether by distillation was recrystallized from benzene, m.p. 164-167°.

3.601 mg substance: 9.662 mg CO_2; 2.038 mg H_2O. Found %: C 73.22; H 6.01. $C_{14}H_{14}O_3$. Calculated %: C 73.05; H 6.08.

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* The attempts made to isolate and purify 4-methoxy-1-chloromethylnaphthalene failed to give positive results, inasmuch as rapid polymerization of this compound takes place when it is vacuum distilled. ** It was found impossible to purify this substance by recrystallization, inasmuch as the compound apparently undergoes partial decarboxylation when it is heated in the recrystallization solvent; after recrystallization the substance melts lower and in a much wider range.

β-1-(4-Hydroxynaphthyl)propionic Acid

A mixture of 1 g of β-1-(4-methoxynaphthyl)propionic acid, 32 ml of hydrobromic acid (d 1.47) and 20 ml of glacial acetic acid was heated for 3 hours under reflux. Then the acids were removed by vacuum distillation; the dark brown residue was dissolved in 10% aqueous NaOH solution and the alkaline solution (after decolorizing with carbon) was acidified with dilute hydrochloric acid. The obtained precipitate (0.6 g) was recrystallized from water. Slightly colored powder, m.p. 125-126°.

2.771 mg substance: 7.311 mg CO_2; 1.448 mg H_2O. Found %: C 72.00; H 5.84. $C_{13}H_{12}O_3$. Calculated %: C 72.22; H 5.55

Methyl Ester of β-1-(4-Hydroxynaphthyl)propionic Acid.

This compound was obtained by heating a mixture of 0.8 g of β-1-(4-hydroxynaphthyl) propionic acid, 45 ml of anhydrous methyl alcohol and 0.3 ml of concentrated sulfuric acid; colorless crystals, m.p. 102.5-103.5° (from petroleum ether-chloroform mixture).

3.610 mg substance: 9.650 mg CO_2; 1.970 mg H_2O. Found %: C 72.95; H 6.10; $C_{14}H_{14}O_3$. Calculated %: C 73.04; H 6.08.

Ethyl Ester of β-1-(4-Hydroxynaphthyl)propionic Acid.

Obtained in the same manner as the methyl ester. After recrystallization frompetroleum ether, m.p. 71.5-73°.

3.513 mg substance: 9.508 mg CO_2; 2.041 mg H_2O. Found %: C 73.86; H 6.50. $C_{15}H_{16}O_3$. Calculated %: C 73.81; H 6.55

β-1-Naphthylpropionic Acid

Into the hydrogenation vessel were charged 20 g of β-1-naphthylacrylic acid, 170 ml of 10% soda solution and 30 g of catalyst (Raney nickel). The hydrogenation was made with slight heating (20-30°). 2270 ml of hydrogen was absorbed. On completion of hydrogenation the catalyst was removed by filtration and the filtrate was acidified with dilute hydrochloric acid. The obtained β-1-naphthylpropionic acid, after recrystallization from ethyl alcohol, had an m.p. of 154-155°. Yield 16 g.

β-2-Naphthylpropionic Acid

1.3 g of β-2-naphthylacrylic acid, 2.6 g of Raney nickel catalyst and 100 ml of ethyl alcohol were shaken in an atmosphere of hydrogen with slight heating of the reaction mixture (20-30°). The theoretical amount of hydrogen (147 ml) was absorbed in 3 hours. After removal of the catalyst the alcohol solution was distilled and the residue was recrystallized from chloroform. β-2-Naphthylpropionic acid has m.p. 131-132°. Yield 0.8 g.

SUMMARY

The new compounds β-1-(4-hydroxynaphthyl) propionic acid and its methyl and ethyl esters were prepared.

LITERATURE CITED

[1] A. Windaus, D. Bernthsen-Buchner, Ber., 50, 1120 (1917).

[2] S. Ruhemann, S. Levy, Ber., 53, 268 (1920).

Received April 2, 1954.

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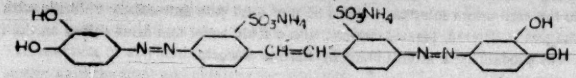
IMPROVED SYNTHESIS OF "STILBAZO" REAGENT

V. I. Kuznetsov and A. A. Nemodruk

The new reagent "stilbazo" – the diammonium salt of stilbene-4,4'-bis(1-azo-3,4-dihydroxybenzene)-2,2'-disulfonic acid, recommended earlier for the colorimetric determination of aluminum [2], is finding increasing practical application [3].



The compound "stilbazo" is of interest for the determination of not only aluminum, but also of some of the other elements. However, the difficult synthesis of "stilbazo" by the originally described method [2] has prevented the widespread use of this valuable reagent.

"Stilbazo" is synthesized by the diazotization of diaminostilbenedisulfonic acid, followed by coupling of the bis-diazo compound with pyrocatechol; at the pH value that is required for the coupling there takes place a secondary reaction involving the oxidation of pyrocatechol by the diazonium salt, which reaction leads to a lower yield of the desired product and to its contamination by the oxidation products of catechol; consequently, in operating with the originally described method it is necessary to carefully purify the product; the yields with this process are about 50%.

After the phenomenon of intramolecular dissociation of cyclic salts was discovered [4], the methods became clear for making it possible to couple azo compounds with pyrocatechol in acid medium, where the pyrocatechol is not oxidized by the diazonium salts [1] This leads to better yields of the desired azo compounds and to their greater purity. Pyrocatechol is capable of coupling with diazonium compounds in acid medium, provided only that it is present as the cyclic aluminum salt, possessing intramolecular dissociation in acid medium [1].

We present an improved method for the synthesis of the reagent "stilbazo", giving yields up to 85%. The synthesis consists of bis-diazotization, coupling, and preparation of the ammonium salt.

EXPERIMENTAL

Diazotization. In 150 ml of water, containing 5 g of anhydrous soda, was dissolved 11.23 g of 87.3% diaminostilbenedisulfonic acid (9.8 g of 100% product corresponds to 0.025 mole); then 3.8 g of $NaNO_2$ was added as a concentrated solution and the solution was filtered from any impurities. The filtered solution with good stirring was slowly poured as a fine stream into a mixture composed of a few pieces of ice, 20 ml of concentrated hydrochloric acid (d. 1.16-1.18), and 20 ml of water. After 30 minutes the reaction mixture, which should give a distinct reaction for nitrous acid, was filtered, and the precipitate of bis-diazo compound pressed and washed with a little water. The product was removed from the funnel and suspended in 50 ml of water.

Coupling. 6.6 g of pyrocatechol (0.06 mole) and 35 g of $KAl(SO_4)_2 \cdot 12H_2O$ were dissolved in 150 ml of water. With good stirring 10 g of anhydrous soda was added and then the suspension of bis-diazo compound was added, with stirring for another 30 minutes. After this, with continued stirring, 100 ml of 20% sodium acetate solution was slowly added dropwise over a period of 2 hours. The reaction mass became dark brown. The stirring was continued for another 2 hours and then 50 ml of concentrated hydrochloric acid was added, either by drops or as a fine stream. After stirring for half an hour the product, appearing as a black deposit, was filtered and very thoroughly washed, first with 3% hydrochloric acid to negative reaction in the wash waters for aluminum (with soda), and then with water. The aluminum-free product was transferred to a beaker, suspended in 700 ml of water, 5 ml of concentrated ammonia added, the mixture stirred for 5-10 minutes and the dark bluish-violet solution filtered from the undissolved residue. With stirring, 50 ml of concentrated hydrochloric acid was added to the filtrate over a period of 1 hour. The obtained dark brown precipitate was filtered and washed with water.

Conversion into the ammonium salt. The conversion of the obtained free acid into the ammonium salt can be realized by two methods:

a) The product is removed from the filter, dried either on the bench or in a vacuum desiccator, finely ground, sifted and the sifted powder poured into a Petri dish to give a layer 5 mm in depth. The dish is placed in a desiccator, on the bottom of which 200 ml of concentrated ammonia is poured. After 1-2 hours the product is taken out, allowed to stand in the air for several hours and then the obtained "stilbazo" reagent is stored. Almost black powder. Yield 14 g (87%) of 97% product. *

b) By the second method the filtered paste of free acid without drying is stirred into 400 ml of water, and ammonia (about 4.5 ml of concentrated ammonia, d. 0.90) is added dropwise to dissolve the product, an excess of ammonia not being permitted, which can be determined by the change in the color of the solution from brown to violet. To the dark brown solution is added 85 g of solid pure ammonium chloride with stirring, the obtained "stilbazo" reagent is filtered, pressed, washed with a little water and dried either on the bench or in a vacuum desiccator. The product is an almost black crystalline powder.

The reagent, obtained by the second method, may be contaminated with a small amount of ammonium chloride, the presence of which fails to impair the quality. The yield of 83% product is 15.2 g (82%).

If the free acid, after the first filtration, is thoroughly washed, the amount of aluminum in the product fails to exceed 0.002 %.

LITERATURE CITED

[1] V. I. Kuznetsov and A. A. Nemodruk, J. Gen. Chem., Suppl. II, 1378 (1953).

[2] V. I. Kuznetsov, G. G. Karanovich, and D. A. Drapkina, Factory Labs., 16, 787 (1950).

[3] P. I. Vasilyev, Methods for the Quick Analysis of Carbonate Deposits, State Geological Press, Moscow, p. 15 (1951); M. Jean, Anal. Chim. Acta. 10, 526 (1954).

[4] V. I. Kuznetsov, J. Gen. Chem., 20, 807 (1950).*

[5] M. V. Gapchenko and O. T. Sheintsis, Factory Labs., 9, 562 (1940).

Received May 17, 1954.

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* See Consultants Bureau English translation, page 845.

* The purity of the product was determined by titration with bivalent vanadium salts [5].

SYNTHESIS OF HYDROXYTETRAHYDROPYRAN AND ITS TRANSFORMATION PRODUCTS

M. I. Farberov, E. P. Tepenitsyna, and N. K. Shemyakina

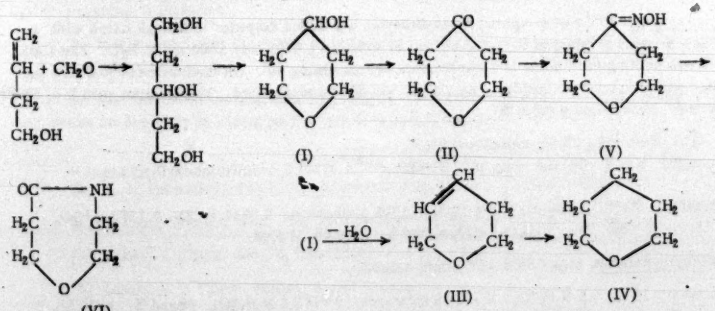
Up to now the derivatives of tetrahydropyran were obtained exclusively from dihydropyran [1]. The latter, in turn, is obtained by the dehydration of tetrahydrofurfuryl alcohol [2]. Baker [3], who passed propylene into a solution of paraform in glacial acetic acid in the presence of 10% sulfuric acid, together with the cyclic formal and butanediol diacetate, obtained 4-acetoxytetrahydropyran in 22.5% yield based on reaction products. The reaction of allylcarbinol with formaldehyde was studied by Olsen [4], who operated however, in glacial acetic acid medium and obtained the triacetate of 1,3,5-pentanetriol as the main product, the transformation of which was studied by him.

In the present study it was shown that the reaction of allylcarbinol with formaldehyde (as formalin solution) in the presence of sulfuric acid gave 4-hydroxytetrahydropyran (I) as the chief reaction product, being obtained in 75% yield.*

Compound (I) was oxidized with chromic anhydride in sulfuric acid, which gave the ketone (II) – tetrahydro-γ-pyrone. This ketone proved to be identical with the ketone obtained by Borsche and coworkers [5] in the hydrogenation of γ-pyrone, which establishes the structure of alcohol (I). The alcohol (I) was dehydrated with $KHSO_4$, which gave 2,3-dihydro-α-pyran (III), which, in turn, was hydrogenated to tetrahydropyran. The obtained tetrahydropyran (IV) proved to be identical with the product described in the literature [6].

In view of the fact that tetrahydro-γ-pyrone (II) is an analog of cyclohexanone, in which the CH_2 group is replaced by oxygen, it was of interest to study its transformation into the lactam.

Treatment of ketone (II) with an alcoholic solution of hydroxylamine gave a quantitative yield of the oxime (V). The obtained oxime was subjected to the Beckmann rearrangement with either p-toluenesulfonyl chloride or 26% oleum to give the lactam of β-ethoxypropionic acid (VI).



The presence of a seven-membered ring in lactam (VI) made it possible to expect its polymerization [7] to the polyamide, having an ether oxygen atom in the ring. However, attempts to polymerize the indicated lactam with different activators at temperatures ranging from 180 to 230° and polymerization periods ranging from 2 to 100 hours, revealed that this lactam is decomposed at high temperatures and does not form polymers. The indicated lactam also fails to give copolymers with ε-caprolactam.**

* The reaction of unsaturated alcohols with aldehydes proved to be a general one, and on this basis we obtained a number of other alcohols – derivatives of tetrahydropyran.

** The experiments on the rearrangement of the oxime into the lactam and on the polymerization of the lactam were made in the laboratory of the Central Scientific Research Institute of Artificial Fibers with the assistance of T. I. Shein and the guidance of Prof. Z. A. Rogovina, to whom we wish to express our deepest gratitude.

The mechanism for the synthesis of hydroxytetrahydropyran from allylcarbinol and formaldehyde is depicted by us in the following manner: in our opinion the first reaction product is 1,3,5-pentanetriol (VII), which is obtained from the reaction of allylcarbinol with formaldehyde in the presence of water. The hydroxyl groups of this triol, found in the 1,5-positions, as is true of all 1,5-diols (δ-glycols), can form δ-oxides with cyclization of the six-membered chain. The formation of δ-oxides readily proceeds in the presence of moderately dilute acids [8]. In the present instance the δ-oxide is 4-hydroxytetrahydropyran (I).

The action of acids can be reduced to the formation of the intermediate carbonium ion [9]:

$$H_2C{=}\overset{\curvearrowright}{O} + H^+ \rightleftharpoons H_2\overset{+}{C}OH \quad (a)$$

$$H_2\overset{+}{C}OH + \overset{\curvearrowleft}{CH_2}{=}CH-CH_2-CH_2OH \rightleftharpoons \underset{OH}{CH_2}-CH_2-\overset{+}{\underset{(b)}{CH}}-CH_2-\underset{OH}{CH_2} \xrightarrow{+HOH^-} (VII) + H^+$$

The acid furnishes a proton for the formation of the carbonium ion (a) from formaldehyde. On the basis of formaldehyde the carbonium ion adds to the double bond of allylcarbinol with the formation of the glycol carbonium ion (b). The latter reacts with water to form the triol (VII) with liberation of the proton.

The application of this mechanism makes it possible to explain why Olsen obtained the triacetate of 1,3,5-pentanetriol from allyl bromide and formaldehyde in glacial acetic acid medium.

As regards the 4-acetoxytetrahydropyran obtained by Baker, then here also, in our opinion, the initial product was allylcarbinol, obtained by the direct reaction of propylene with formaldehyde [10]. On further reaction with formaldehyde by the indicated mechanism the tetrahydropyran derivative was obtained.

EXPERIMENTAL

4-Hydroxytetrahydropyran. 72 g of allylcarbinol, 30 g of formaldehyde (73 ml of solution containing 40 g/100 ml) and 2.2 ml of H_2SO_4 (d_4^{20} 1.82) were charged into a round-bottom flask with reflux condenser and heated for 3 hours. After completion of reaction the mixture was neutralized with saturated soda solution and distilled. The fraction with b.p. 97-97.5° at 25 mm was collected. Yield 76.38 g (74.8%). The compound is soluble in water.

B.p. 190° (760 mm), n_D^{20} 1.4612, d_4^{20} 1.0708, MR_D 26.20; calculated 26.25.

M.p. of the dinitrobenzoate (from alcohol) 155.5-160°.

Found %: C 58.25, 58.63; H 10.23, 9.76; OH (phthalation) 15.7. $C_5H_{10}O_2$. Calculated %: C 58.80; H 9.87; OH 16.68.

Tetrahydro-γ-pyrone. 177 g of 4-hydroxytetrahydropyran was added dropwise to a flask fitted with a stirrer and containing a mixture of 360 g of $K_2Cr_2O_7$, 200 ml of H_2SO_4 (d 1.810), and 1500 ml of H_2O. The flask contents were stirred with cooling for 6 hours at a temperature not exceeding 30°. On conclusion of reaction the mixture was extracted with ethylene dichloride. The extract was dried and distilled. The fraction with b.p. 67-68° at 18 mm was collected. Yield 46.42 g (26.8%).

n_D^{20} 1.4510, d_4^{20} 1.0844, MR_D 25.00; calculated 24.75.

Literature data [5]: b.p. 67-69° (18 mm), $n^{24.5}$ 1.4529, $d^{24.5}$ 1.0795; 2,4-dinitrophenylhydrazone – m.p. 186-187°.

0.1345 g substance: 0.2921 g CO_2; 0.0958 g H_2O. 0.1708 g substance: 0.3741 g CO_2; 0.1170 g H_2O. Found %: C 59.44, 59.77; H 7.96, 7.66. $C_5H_8O_2$. Calculated %: C 59.66; H 8.06.

2,4-Dinitrophenylhydrazone, m.p. 186.5-187° (from alcohol).

0.1527 g substance: 13 ml 0.1 N H_2SO_4. 0.1086 g substance: 9 ml 0.1 N H_2SO_4. Found %: N 20.20, 19.75. $C_{11}H_{12}O_5N_4$. Calculated %: N 20.00.

Tetrahydro-γ-pyrone oxime. 40 g of tetrahydropyrone was added to an alcohol solution of hydroxylamine (35 g $NH_2OH \cdot HCl$ + 60 ml C_2H_5OH + 320 ml H_2O). The mixture was heated to 75° and then stirred for 24 hours. On conclusion of reaction the mixture was neutralized with 50% NaOH, extracted with ether, and the extract distilled. Tetrahydropyrone oxime distills at 97-100° at 6 mm. The yield of product is quantitative. B.p. 99-100° at 6 mm. M.p. 87.5°; colorless needlelike crystals. (From the literature [5], m.p. 87-88°).

0.1270 g substance: 13 ml N_2 (24°, 754 mm); 0.1685 g substance: 17.8 ml N_2 (23°, 760 mm). Found %: N 11.8, 12.08. $C_5H_9O_2N$. Calculated %: N 12.18.

2,3-Dihydro-α-pyran. A mixture of 70 g of 4-hydroxytetrahydropyran and 70 g of freshly fused $KHSO_4$ was heated in a flask, connected to a fractionation column. The azeotrope with b.p. 78-80° was collected. The top layer after drying was distilled. Yield of product 33 g (57.2%).

B.p. 93° (760 mm), n_D^{24} 1.4480, d_4^{24} 0.9394, MR_D 23.93; calculated 24.26.

0.1239 g substance: 0.3234 g CO_2; 0.1029 g H_2O. 0.1865 g substance: 0.4852 g CO_2; 0.1616 g H_2O. Found %: C 71.21, 71.06; H 9.4, 9.7. C_5H_8O. Calculated %: C 71.42; H 9.52.

Tetrahydropyran. 20.2 g of 2,3-dihydro-α-pyran was hydrogenated at normal pressure in the presence of 2 g of catalyst (5% Pd on activated charcoal). The yield was quantitative.

B.p. 87.5° (764 mm), n_D^{20} 1.4205, d_4^{20} 0.8853. Literature data [6]: b.p. 88° (760), $n_D^{18.5}$ 1.4195, d_4^{15} 0.8853.

β-Ethoxypropionic acid lactam. The rearrangement of the oxime into the lactam was done by two methods:

1) To a solution of 11.5 g of oxime in 70 ml of 5 N NaOH, heated on the water bath, was gradually added with stirring 19 g of p-toluenesulfonyl chloride. The temperature was raised to 110-120°. The cooled reaction mixture with precipitate was extracted with chloroform. The extract after drying and removal of the chloroform was vacuum distilled in a current of nitrogen. B.p. 165° at 15 mm. Yield of product was 2.25 g (20%).

2) A solution of 25 g of oxime in 50 ml of ethylene dichloride was simultaneously added with 18 ml of 25% oleum to the reaction flask over a period of 35 minutes. Then the mixture was cooled, neutralized with ammonia, and the water layer extracted with chloroform. The extract after drying was distilled. The yield of lactam was 30%. The molecular weight of the lactam was determined from the amino acid that was obtained when the lactam was hydrolyzed with 2% H_2SO_4 solution at the boil for 3 hours. The amino acid was titrated with 0.1 N NaOH solution in the presence of 30% formalin.

Found M 132.73. $C_6H_{11}O_3$. Calculated M 133.0. Lactam: m.p. 82.5-83.0°.

Found %: C 53.0; H 7.9; N 12.08. $C_5H_9O_2N$. Calculated %: C 52.1; H 7.8; N 12.18.

SUMMARY

1. The smooth course of the reaction between allylcarbinol and formaldehyde in the presence of acids, leading to the formation of 4-hydroxytetrahydropyran, was shown.

2. Some transformation products of 4-hydroxytetrahydropyran were prepared, in which number tetrahydro-γ-pyrone is included.

3. It was shown that the oxime of tetrahydro-γ-pyrone is rearranged with ring cleavage into the lactam of β-ethoxypropionic acid.

4. The indicated lactam, differing from ε-caprolactam in that it has ether oxygen in a seven-membered ring, shows no tendency to either polymerize or to copolymerize.

LITERATURE CITED

[1] A. L. Ponomarev and V. V. Zelenkova, Prog. Chem., 20, 589 (1951).

[2] R. Paul, Compts, rend. 196, 1409 (1933); Bull Soc. Chim., 53, 1480 (1953).

[3] Baker, J. Chem. Soc., 6, 296 (1944).

[4] Olsen, Acta Chem. Scand., 6, 641 (1952).

[5] Borsche, Ber., 48, 688 (1918); 56, 2012 (1923).

[6] Paul, Bull. Soc. Chim., 53, 1493 (1933); Allen, Hibbert, J. Am. Chem. Soc., 56, 1398 (1934).

[7] I. L. Knunyants, Z. A. Rogovin, Yu. Rymashevskaya, and E. V. Khaut, J. Gen. Chem., 17, 987 (1947); 17, 1321 (1947).

[8] Delepine, Ann. Chim., 7, 378; Adkins, J. Am. Chem. Soc., 47, 1368 (1925).

[9] Price. Mechanisms of reactions of carbon-carbon double bonds, New York 44 (1946).

[10] Arundale, Mikeska, Chem. Revs., 51, 505 (1952); Prog. Chem., 23, 223 (1954).

Received April 24, 1954.

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STEREOISOMERISM OF OXIMES AND HYDRAZONES

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The geometric isomerism of the oximes of aldehydes and unsymmetrical ketones has been quite extensively studied [1, 2].

As a rule, in the case of aliphatic aromatic ketones only one form of the oxime is obtained. The literature on the Beckmann rearrangement of such ketoximes reveals that they have the configuration of the syn-alkyl oxime. The rearrangement of such ketoximes always results in the formation of aromatic amine and aliphatic acid:

$$X-C_6H_4-\underset{\underset{N-OH}{\|}}{C}-Alk \longrightarrow X-C_6H_4-NH_2 + Alk-COOH$$

Here X = H, CH_3, Cl, Br, NO_2, while Alk = CH_3 [3], C_2H_5 [4], C_3H_7 [5], and $C(CH_3)_3$ [6]; the alkyl radical can also contain halogen [7, 8], CH_3CO group [9] and C_6H_5 [10, 11].

The oximes of aliphatic ketones are usually oils that can be purified only with difficulty. During Beckmann rearrangement they form a mixture of two amines and two acids [12]. Apparently, they are a mixture of both geometric isomers. These facts can be explained in the following manner: in their relation to the electron cloud the different alkyls differ but slightly from each other; consequently, they exert approximately the same influence on the hydroxyl group of hydroxylamine at the time of oxime formation; both geometric isomers are formed in approximately equal amounts, and their stability is approximately the same. The unsymmetrically substituted benzophenones differ from the unsymmetric aliphatic ketones in that here, due to the greater polarity of benzene rings, the substituents markedly alter the character of the C_6H_4X radical; consequently the isomer that will be formed in greatest amount is the one for which the energy of formation conditions are most favorable. This isomer proves to be stable.

In some cases the character of the substituent changes when the medium is changed; in such case a change can also take place in the relative stability of the geometric isomers that are formed.

Thus, o-aminobenzophenone forms 2 stereoisomeric oximes, of which the anti-phenyl oxime proves to be stable in the free state or in alkaline solution, while the syn-phenyl oxime (m.p. 127°) is stable in acid solution [13]. The geometric configuration of these oximes is proved by Beckmann rearrangement [14], and also by the fact that only the anti-phenyl oxime (I) on diazotization is converted into 3-phenylbenzisoxazole [15].

In a similar manner, insofar as the pyridine nucleus attracts electrons more strongly than does the benzene ring, phenyl α-pyridyl ketone forms a stabile syn-phenyl oxime and a labile anti-phenyl oxime [16].

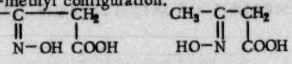
In aliphatic aromatic ketones the difference between radicals in the examined sense is extremely great; consequently, as was already indicated above, these ketones form, as a rule, only one oxime. At first it was assumed that the stereoisomerism of oximes was peculiar only to purely aromatic ketones. In 1897, i.e., 15 years after the discovery of oximes, it was found that phenyl cyclohexyl ketone forms two geometric isomers [17]. In 1950 for the first time two geometric isomers of the oxime of an aliphatic aromatic ketone – isobutyrophenone – were obtained [18]. In this case also the syn-isopropyl oxime (m.p. 96°), as was to be expected, proved to be the stabile isomer, while its anti-isomer (m.p. 90°) was the labile form.

A comparatively long time ago attempts were made to arrange the radicals in the order of their influence on the distribution of the hydroxyl group in unsymmetrical ketoximes [19, 20]. However, at the time an erroneous opinion existed on the mechanism of the Beckmann rearrangement of ketoximes [12].

Thus, according to Hantzsch, the oxime of acetoacetic acid should have the space configuration of the anti-methyl oxime (I).

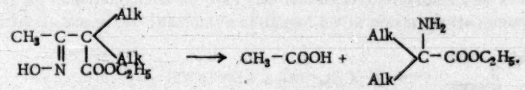
With such a configuration, the oxime should readily undergo cyclization into the ixoxazolone ring. Taking this into consideration, Hantzsch postulated that the "methylisoxazolone" obtained by him is transformed in water solution into the oxime of acetoacetic acid, and that when the product is removed from solution it immediately forms anew the isoxazolone ring.

The error of such a representation has been demonstrated at the present time. First, the methylisoxazolone obtained by Hantzsch is actually the dicyclic heterocycle dimethyloxydiisoxazolyl [21]; second, the oxime of acetoacetic acid (II) synthesized by us proved to be completely stable and incapable of cyclizing to the hetero ring [22]. This can be explained only by its syn-methyl configuration.



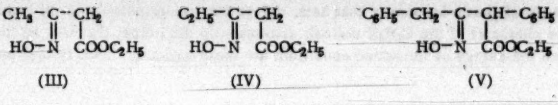
(I) (II)

Unfortunately, the oximes of acetoacetic acid and its ester do not lend themselves to the Beckmann rearrangement; when this is done the structure of the rearrangement products indicates the syn-methyl configuration of these oximes [23].

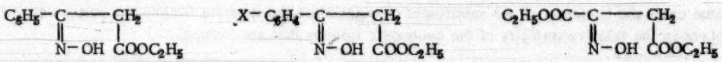


The oxime of the propionylacetic ester (IV) also shows the same behavior as the oxime of acetoacetic ester (III). Our experiments revealed that it forms the isoxazolone compounds (more to the point, also bicyclic) with extreme difficulty and in very low yield. The oxime of α,γ-diphenylacetoacetic ester (V) [24] is characterized by a similar behavior. On the other hand, the oxime of oxalacetic ester (VIII) is very readily transformed into the ester of isoxazolonecarboxylic acid [25]. In this respect it behaves like the oxime of the benzoylacetic ester (VI) and its derivative (VII).

As a result, not only the Beckmann rearrangement, but also the difference in the ease of heterocycle formation from the oximes of β-keto acids and their esters show that the latter possess a different space structure.



(III) (IV) (V)



(VI) (VII) (VIII)

From these examples we see that in unsymmetrical ketoximes, obtained in the form of one isomer, the hydroxyl group is turned toward the more electron donor radical. As has already been said above, in those cases where it is possible to obtain both geometric isomers of the oxime, in the stabile isomer the hydroxyl is also turned toward the more electron donor radical.

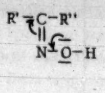
In the corresponding hydrazones there exists, it might be said, the same C=N grouping (serving as the center of geometric isomerism), and consequently it could be expected that they also would have the same stereochemical rules. However, in practice it was shown that the acetoacetic and benzoylacetic esters when reacted with phenylhydrazine undergo ring closure to form the pyrazolone derivative with approximately the same degree of ease. The questions arise: why is the ease of closing the pyrazolone ring independent here of the character of the radical that is bound to the carbonyl group of the β-keto acid, while in the case of closing the isoxazolone ring such a relation is present? Why is the postulation on the absence of free rotation around the double bond C=N supported in the cases where the oximes undergo ring closure to form pyrazolones and not supported in the closure of hydrazones to yield pyrazolones?

A study of the facts, relating to the geometric isomerism of oximes and hydrazones reveals that in the case of the oximes this phenomenon is very frequently encountered, while at the same time it is absent in the case of unsubstituted hydrazones. However, the individual cases of geometric isomerism of substituted hydrazones reveal that the postulation on the absence of free rotation around the C=N double bond should be limited to certain hydrazones. Up to now a theoretical consideration of the question has not been made: why do hydrazones so rarely manifest geometric isomerism and in what specific cases can we expect the formation of two stereoisomeric hydrazones?

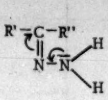
It is most natural to assume that the difference in the sterochemical properties of oximes and hydrazones is due to the difference in the resonance of the C=N double bond, that the rotation around this bond in the case of

hydrazones is usually less difficult than in the case of the oximes. The stereochemical theory has nothing to say on the quantitative aspects of the matter. Dealing for the most part with the geometry of isomeric molecules, this theory considers this "resonance" of molecules in a class separate from the whole molecule, neglecting to take into account the influence of the other atoms and groups present in the molecule.

In oximes and hydrazones with similar structures (IX and X) the influence of the OH and NH_2 groups on the C=N double bond is expressed in the shifting of the unshared electrons of these groups toward the nitrogen of the C=N group and in the induced displacement of the π-electrons of the C=N group toward the carbon (induction effect). Schematically, with the aid of curved arrows, this can be depicted in the same manner for both oximes (IX) and hydrazones (X):



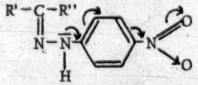
(IX)



(X)

However, for hydrazones this displacement should be more pronounced than it is for oximes, as a result of which the nitrogen has a lower affinity than oxygen for electrons. Limiting ourselves to the induction effect, which usually appears as the dominating factor in the mutual influence of atoms when mobile electrons are present in the chain, it can be said that the greater induction effect of the NH_2 group in hydrazones when compared to the OH group in oximes leads to such a marked decrease in the double bond nature of the C=N bond in hydrazones that rotation around this bond is no longer difficult. This can be considered as being the main reason for the stereochemical characteristics of oximes (IX) and hydrazones (X) with similar structures, inasmuch as in their chemical structure they differ from each other only in the OH and NH_2 groups, which are united to nitrogen atoms in otherwise completely identical molecules. If this postulation is valid, then the double bond nature of the C=N in hydrazones can be raised by the introduction of such a substituent in the NH_2 group as will cause the unshared pair of electrons, present in this group, to shift in the opposite direction; consequently, it can be expected that the introduction of nitro groups in the ortho- and para-positions of the phenyl radical in the phenylhydrazone molecule will increase the possibility of obtaining the geometric isomers of such hydrazones.

The influence of the nitro group, for example, found in the para-position, can be depicted in the following manner:



At the present time a very large number of 4-nitrophenylhydrazones and 2,4-dinitrophenylhydrazones of different aldehydes and ketones have been prepared and described. A study of this material leads to the conclusion that one nitro group, found in the 4-position, is still not sufficient to raise the "resonance" of the C=N bond to the point of geometric isomerism appearance. In the presence of two nitro groups in the 2- and 4-positions the geometric isomerism of hydrazones already becomes possible in certain cases.

As a rule, the p-nitrophenylhydrazones are obtained in very high yields and with well-defined constants [26]. In the literature no mention is made of the existence of geometric isomers of these compounds. The 2,4-dinitrophenylhydrazones and 2,4,6-trinitrophenylhydrazones at times are formed as two isomers [27, 28, 29]. Also, there are indications that in many cases the 2,4-dinitrophenylhydrazones are obtained with ill-defined melting points, which vary depending on their preparation conditions [29, 30].

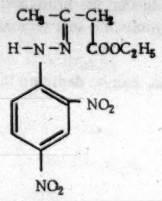
These facts can be considered as offering some support to the above made postulations, the validity of which we decided to establish by way of studying the ease of forming the pyrazolone ring from the phenylhydrazones of acetoacetic and benzoylacetic esters, containing different amounts of nitro groups in the 2-, 4- and 6-positions. The results of this study are given in the table.

On comparing the results given in the table, it is evident that the hydrazones of acetoacetic ester in all five cases are transformed into pyrazolones with greater difficulty than the corresponding hydrazones of benzoylacetic ester. Here also, as in the case of the oximes, the CH_3 group hinders, and the C_6H_5 group facilitates closure of the heterocycle. If the opposite influence of these groups was practically almost undetectable in the reactions of acetoacetic and benzoylacetic esters with phenylhydrazines, then in the reactions with the nitrated phenylhydrazines it becomes more noticeable. This difference is especially clear in the reactions with 2,4-dinitrophenylhydrazine:

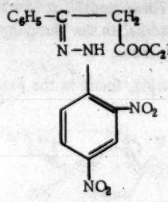
Starting compound	Position of nitro group in phenylhydrazone	–	3	4	2 and 4	2, 4 and 6
$CH_3-CO-CH_2-COOC_2H_5$	Possibility of obtaining the hydrazone	+	+	+	+	+
	Conditions for the closure of the pyrazolone ring	100°	140-150°	175-180°	H_2SO_4 55-60°	H_2SO_4 100°
$C_6H_5-CO-CH_2-COOC_2H_5$	Possibility of obtaining the hydrazone	–	–	–	–	+
	Conditions for the closure of the pyrazolone ring	In the formation of the hydrazone				H_2SO_4 20°

with acetoacetic ester the latter forms a hydrazone, which by heating can in no way be converted into the pyrazolone, while with benzoylacetic ester the pyrazolone is readily formed and it is found impossible to stop the reaction at the hydrazone stage. As in the case of the oximes, we believe the possible explanation for this lies in the influence of the space factor, depending on the spatial arrangement of the hydrazone molecule to the radical (CH_3 or C_6H_5) that is attached to the carbonyl group of the starting ester.

Thus, the 2,4-dinitrophenylhydrazone of acetoacetic ester (XI) is the syn-methyl hydrazone. In it the "resonance" of the C=N bond prevents the approach of the NH and $COOC_2H_5$ groups.



(XI)



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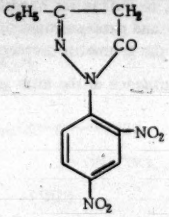
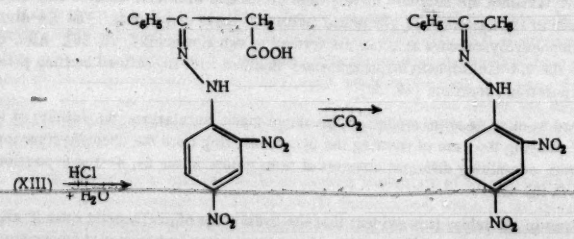


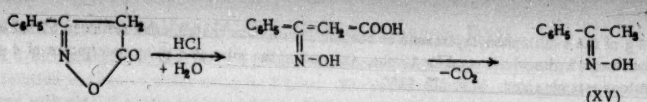
(XIII)

From benzoylacetic ester the 2,4-dinitrophenylhydrazone is formed as the anti-phenyl isomer (XII). In it the "resonance" of the C=N bond does not prevent the approach of the NH and $COOC_2H_5$ groups, and it is immediately converted into the pyrazolone (XIII). It was revealed that the pyrazolone (XIII) decomposes when heated with concentrated hydrochloric acid and is transformed into the 2,4-dinitrophenylhydrazone of acetophenone (XIV).



(XIV)

The other pyrazolones synthesized by us, containing two or three nitro groups in the 2-, 4- and 6-positions of the phenyl radical, also suffer cleavage in similar manner. In this respect they bear a resemblance to phenylisoxazolone, which compound is cleaved in a similar manner when heated with concentrated hydrochloric acid [31].



(XV)

That the acetophenone oxime (XV) obtained in this manner is the syn-methyl isomer is confirmed by the Beckmann rearrangement reaction. Hydrazones are incapable of such rearrangement; consequently, the solitary chemical criterion of the spatial configuration of hydrazone (XIV) is its genetic relation to the pyrazolone (XIII). However, this criterion would be fully convincing only if it were possible to obtain the 2,4-dinitrophenylhydrazone of acetophenone in the form of two geometric isomers.

We were able to find such reaction conditions that acetophenone gave two isomers of the 2,4-dinitrophenylhydrazone derivative, the already known red isomer with m.p. 244-246° (stabile), and a new yellow isomer with m.p. 147-147.5° (labile). Treatment of pyrazolone (XIII) with hydrochloric acid gives the red isomer. The yellow isomer is not converted to the red form under these conditions; consequently, to the red isomer we can assign the configuration of the anti-phenyl hydrazone, and to the yellow, the syn-phenyl hydrazone. The yellow isomer can be readily changed into the red form. This transformation takes place when the yellow isomer is heated above its melting point, best of all at 240-245°; by heating the yellow isomer in glacial acetic acid at the boil; by prolonged standing of a solution of the yellow isomer in concentrated sulfuric acid at room temperature; by dissolving the yellow isomer in alcoholic NaOH with subsequent acidification of the cherry-red alkaline solution. We were unable to realize the reverse transition from the red isomer to the yellow. As a result, the red isomer is the stabile form, while the yellow isomer is the labile form.

Inasmuch as in the preparation of the hydrazone both isomers are simultaneously formed under diverse conditions, and inasmuch as neither is converted into the other when both isomers are recrystallized from the same solvent (for example, alcohol or pyridine), then dimorphism in the given case is excluded.

The ultraviolet absorption spectra of these isomers support the fact that here we have true geometric isomerism, and not structural isomerism: the obtained spectra hardly differ in the shape of the curves; only the absorption maximum for the yellow isomer (λ_{max} = 365 A) is shifted by 10 A toward the short wave lengths when compared to the maximum for the red isomer (λ_{max} = 375 A).

The syn-phenyl hydrazone differs from the anti-isomer by a tighter spatial arrangement, resulting in disturbance of the planar structure of the molecule. The greater solubility of the yellow isomer, as well as its lower melting point, agree with the rule postulated by I. Kiprianov: "The melting points of compounds with a nonplanar molecule are considerably lower than for analogous compounds with planar molecules. The spatially hindered dyes are more soluble in alcohol" [32]. The deeper color of the syn-phenyl hydrazone when compared to the anti-phenyl hydrazone is also found to be in agreement with the existing rule, which, according to Terenin, supports the statement that "disturbance of the planar arrangement and deformation of the molecule is usually accompanied by a distinct hypsochromic effect, i.e., by a shifting of the absorption bands toward the short wave lengths" [33].

In conclusion it might be mentioned that in recent years some new cases of geometric isomerism of the 2,4-dinitrophenylhydrazones of unsymmetrical ketones (p-chlorobenzophenone [34], methyl isopropyl ketone [35], and phenyl α-pyridyl ketone [16]) have been discovered. Inasmuch as the mononitrophenylhydrazones and the unsubstituted phenylhydrazones of these ketones do not form geometric isomers, these facts speak in favor of the above presented hypothesis.

EXPERIMENTAL

Preparation of 4-Nitrophenylmethylpyrazolone

The starting 4-nitrophenylhydrazone of acetoacetic ester was obtained by heating the reagents for 2 hours on the boiling water bath. Yield 74 %, m.p. 117.5-118.5° (cor.) [36]. Our experiments failed to support the statement made by Altschul [37] that this hydrazone melts when heated on the water bath, splits off alcohol and is converted into the pyrazolone. This hydrazone melts at 117° without the cleavage of alcohol. At 175-180° gas bubbles are evolved and the mass hardens. The substance is recrystallized from alcohol and from glacial acetic acid, after which it has m.p. 217-218° and fails to lower the melting point when mixed with known 4-nitrophenylmethylpyrazolone.

a) 1.0 g of the 4-nitrophenylhydrazone of acetoacetic ester was dissolved in 5 ml of sulfuric acid (d 1.84). The solution was allowed to stand for 1 hour at 20-25° and was then poured into 300 ml of water. 10 g of sodium bicarbonate was carefully added to give a white precipitate, which was filtered, washed with water until neutral, and dried. Yield 0.7 g. After recrystallization from 10 ml of glacial acetic acid the compound has m.p. 216-217° and is 4-nitrophenylmethylpyrazolone.

b) 1.0 g of the 4-nitrophenylhydrazone of acetoactic ester was heated under reflux in 50 ml of alcohol with 1 ml of concentrated hydrochloric acid for 1 hour. On cooling the solution a shiny precipitate of 4-nitrophenylmethylpyrazolone was obtained. M.p. 215-216°.

Preparation of 2,4-Dinitrophenylmethylpyrazolone

The starting 2,4-dinitrophenylhydrazone of acetoactic ester was obtained by heating the reagents in boiling alcohol, acidified with hydrochloric acid, for 1 hour. Yield 74%, m.p. 91.5-92.5° (cor.) [38, 39].

a) 1.0 g of this hydrazone was heated in a test tube with thermometer. At 91-92° the substance became an orange colored liquid, which on further heating gradually darkened. At 198-205° the liquid began to decompose: gas bubbles were evolved and the liquid was transformed into a black tarry mass, which failed to solidify on cooling. This method cannot be used for the preparation of the pyrazolone.

b) 1.0 g of the 2,4-dinitrophenylhydrazone of acetoacetic ester was dissolved in 5 ml of sulfuric acid (d 1.84). The solution was allowed to stand for 1 hour at 20-25° and was then poured into 300 ml of water. The careful addition of 10 g of sodium bicarbonate gave an orange precipitate, which was filtered, washed with water until neutral, and dried. Yield 0.8 g. After recrystallization from alcohol the substance has m.p. 91-92° and is the unchanged 2,4-dinitrophenylhydrazone of acetoacetic ester. These conditions also fail to achieve closure of the pyrazolone ring.

c) 1.0 g of the 2,4-dinitrophenylhydrazone of acetoacetic ester was dissolved in 8 ml of sulfuric acid (d 1.84). The solution was heated on the water bath for 1 hour at 55-60°, then cooled and poured into 300 ml of water. Careful neutralization of the solution with sodium bicarbonate gave a yellow precipitate, which was filtered, washed with water, and dried. Yield 0.4 g. After two recrystallizations from 20 volumes of alcohol the substance melts at 144-144.5° (cor.) and is 2,4-dinitrophenylmethylpyrazolone.

0.1093 g sub.: 0.1815 g CO_2; 0.0328 g H_2O. 0.1126 g sub.: 21.2 ml N_2 (24°, 751 mm). 0.1136 g sub.: 21.6 ml N_2 (24°, 742 mm). Found %: C 45.29; H 3.33; N 21.14, 21.11. $C_{10}H_8O_5N_4$. Calculated %: C 45.45; H 3.03; N 21.21.

Preparation of 2,4,6-Trinitrophenylmethylpyrazolone

The starting 2,4,6-trinitrophenylhydrazone of acetoacetic ester was obtained by heating 1.0 g of 2,4,6-trinitrophenylhydrazine and 10 ml of acetoacetic ester on the boiling water bath for 4 hours. 60 ml of alcohol was added to the cooled solution and then 15 ml of water was carefully added. After several hours a brownish precipitate was obtained. This precipitate was filtered, washed with water, and dried. Yield 35%, m.p. 113-115 [38, 39]. We were unable to obtain 2,4,6-trinitrophenylmethylpyrazolone under the earlier described conditions (a, b and c above) used for the preparation of 2,4-dinitrophenylmethylpyrazolone.

d) The heating of the 2,4,6-trinitrophenylhydrazone of acetoacetic ester in concentrated sulfuric acid at 100° for 1 hour led to the formation of 2,4,6-trinitrophenylmethylpyrazolone: 2.0 g of the 2,4,6-trinitrophenylhydrazone of acetoacetic ester was dissolved in 10 ml of concentrated sulfuric acid. The cherry-red solution was heated on the boiling water bath for 1 hour. The cooled solution was poured into 200 ml of water and then sodium bicarbonate was carefully added to weakly acid reaction to Congo paper. The obtained yellowish precipitate was filtered, washed with water, and dried. Yield 1.6 g (92%). For purification the substance was recrystallized twice from 10-fold amounts of glacial acetic acid. Pure 2,4,6-trinitrophenylmethylpyrazolone is light yellow in color and melts at 211-212° (cor.). The compound can be recrystallized from 1000 parts of boiling water.

0.1236 g sub.: 0.1752 g CO_2; 0.0280 g H_2O. 0.0969 g sub.: 19.8 ml N_2 (22°, 740 mm). Found %: C 38.66; H 2.52; N 22.80. $C_{10}H_7O_7N_5$. Calculated %: C 38.83; H 2.27; N 22.65.

Reaction of Phenylhydrazine with Benzoylacetic Ester

1 ml of phenylhydrazine and 2 ml of benzoylacetic ester were dissolved in 10 ml of glacial acetic acid. The solution was heated under reflux for some time and then cooled. A light yellow precipitate of 1,3-diphenylpyrazolone was obtained. Yield 0.65 g (30%); m.p. 137-137.5° (cor.). The same substance is formed when equivalent amounts of phenylhydrazine and benzoylacetic ester are mixed [40].

Reaction of 3-Nitrophenylhydrazine with Benzoylacetic Ester

We carried out the reaction in accord with the literature indications [41] and obtained 1-(3'-nitrophenyl)-3-phenyl-5-pyrazolone as pale yellow needles with m.p. 174°. As a result, in the given case also it is impossible to obtain the hydrazone of benzoylacetic ester, inasmuch as the corresponding pyrazolone is immediately formed.

Reaction of 4-Nitrophenylhydrazine with Benzoylacetic Ester

1.53 g of 4-nitrophenylhydrazine and 2.6 ml of benzoylacetic ester were dissolved in 20 ml of glacial acetic acid and the solution was heated under reflux for 3 hours. The yellow precipitate that separated on cooling was filtered, washed with glacial acetic acid, and dried. Yield 1.8 g (64%). For purification 1-(4'-nitrophenyl)-3-phenyl-5-pyrazolone was recrystallized twice from 40 parts of ethyl acetate. M.p. 207.5-208° (cor.). The same results are obtained when the reaction is carried out in alcohol solution in the presence of several drops of concentrated hydrochloric acid.

0.1043 g sub.: 0.2444 g CO_2; 0.387 g H_2O. 0.0956 g sub.: 12.9 ml N_2 (25°, 746 mm). 0.0020 g sub.: 0.0298 g camphor; Δt 9.8°. Found %: C 63.91; H 4.12; N 15.00. M 274. $C_{15}H_{11}O_3N_3$. Calculated %: C 64.06; H 3.91; N 14.95. M 281.

Reaction of 2,4-Dinitrophenylhydrazine with Benzoylacetic Ester

1.0 g of 2,4-dinitrophenylhydrazine, 1.34 g of benzoylacetic ester, 20 ml of alcohol and 3 drops of concentrated hydrochloric acid were heated under reflux for 10 minutes. A copious, yellow-orange, lustrous precipitate of 1-(2',4'-dinitrophenyl)-3-phenyl-5-pyrazolone was obtained. The precipitate was filtered, washed with alcohol, and dried. Yield 1.6 g (about 100%); m.p. 160-161°. After recrystallization from 10 parts of glacial acetic acid the melting point remains constant. 1.0 g of the substance dissolves in 500 ml of boiling alcohol, and in 25 ml of boiling ethyl acetate.

0.0664 g sub.: 0.1346 g CO_2; 0.0202 g H_2O. 0.675 g sub.: 9.8 ml N_2 (20°, 770 mm). 0.0017 g sub.: 0.0399 g camphor: Δt 5.2°. Found %: C 55.28; H 3.38; N 16.99. M 327.7. $C_{15}H_{10}O_5N_4$. Calculated %: C 55.21; H 3.07; N 17.18. M 326.

Reaction of 2,4,6-Trinitrophenylhydrazine with Benzoylacetic Ester

3.24 g of trinitrophenylhydrazine, 2.4 ml of benzoylacetic ester, 60 ml of alcohol and 12 drops of concentrated hydrochloric acid were heated under reflux with mechanical stirring for 1 hour. A red precipitate of the 2,4,6-trinitrophenylhydrazone of benzoylacetic ester was obtained. The precipitate was filtered, washed with alcohol, and dried. Yield 3.15 g (57%). The compound was recrystallized from 150 volumes of alcohol. M.p. 146-147° (cor.).

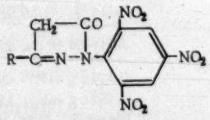
0.1047 g sub.: 0.1868 g CO_2; 0.0367 g H_2O. 0.1085 g sub.: 16.3 ml N_2 (23°, 754 mm). Found %: C 48.66; H 3.89; N 17.03. $C_{17}H_{15}O_8N_5$. Calculated %: C 48.92; H 3.60; N 16.78.

Preparation of 1-(2',4',6'-Trinitrophenyl)-3-phenyl-5-pyrazolone

1.0 g of the trinitrophenylhydrazone of benzoylacetic ester was dissolved in 5 ml of concentrated sulfuric acid and allowed to stand for 1 hour at 20°. The solution was poured into 200 ml of water. The yellow precipitate was filtered, washed with water, and dried. Yield 0.85 g (95%). The substance can be recrystallized from 25 parts of glacial acetic acid or from 100 parts of alcohol. M.p. 223.5-224° (cor.).

0.1011 g sub.: 0.1790 g CO_2; 0.0234 g H_2O. 0.1063 g sub.: 17.9 ml N_2 (22°, 748 mm). Found %: C 48.29; H 2.53; N 19.03. $C_{15}H_9O_7N_5$. Calculated %: C 48.52; H 2.43; N 18.87.

Influence of Concentrated Hydrochloric Acid on di- and Trinitrophenylpyrazolones of the General Formula



R = CH_3 or C_6H_5

A small amount (~0.5 g) of the di- or trinitrophenylpyrazolone was boiled with concentrated hydrochloric acid (5-50 ml) for 20-30 minutes. When necessary the hot solution was filtered through cotton batting. The reaction product separated on cooling the solution or after diluting it with water. When R = CH_3 the reaction products are the dinitrophenylhydrazone of acetone (m.p. 125-125.5°, cor.) and the trinitrophenylhydrazone of acetone (m.p. 126-127°). When R = C_6H_5 the reaction products are the dinitrophenylhydrazone of acetophenone (m.p. 244-246°, cor.) and the trinitrophenylhydrazone of acetophenone (m.p. 252-252.5°, cor., with decomposition). To identify the obtained compounds the indicated hydrazones were synthesized from the corresponding ketones. No depression of the melting point was observed for the mixtures of obtained substances and known hydrazones.

Preparation of the Red and Yellow Isomers of Acetophenone 2,4-Dinitrophenylhydrazone

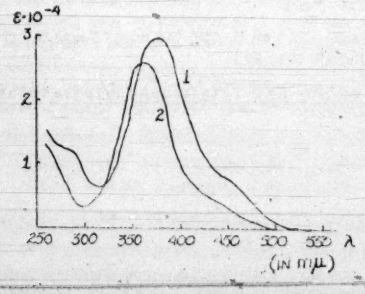
a) 4.0 g of dinitrophenylhydrazine and 10.6 ml of acetophenone were heated on the hot plate in a flask fitted with an air condenser. Gradually the whole mass went into solution and the liquid began to boil, the boiling continuing for some time due to the exothermic nature of the started reaction. The boiling was continued for 10 minutes; the reaction water, condensing in the tube and falling back into the boiling liquid, produced the characteristic sputtering; then a red crystalline precipitate began to separate. After this the liquid with the precipitate was maintained for 10 minutes at a slight boil in the open flask for removal of the water. The mixture was heated until complete solution of the precipitate had been obtained and then it was allowed to stand at room temperature for 20-25 hours. The glistening red needles thus obtained were filtered and washed with 5 ml of alcohol. Yield 5.0-5.3 g (83-88%); m.p. 244-246° (cor.), with slight decomposition.

70 ml of alcohol and 40 ml of water were added to the filtrate. If some oily drops of acetophenone were obtained on adding the water, then they were put back into solution by adding a small amount of alcohol. Soon the solution became turbid, and a yellow crystalline precipitate was deposited. The precipitate was filtered and washed with alcohol. Yield 0.30-0.35 g (5-6%); m.p. 145.5-146.5° (cor.). The alcohol-water-acetophenone filtrate was used for precipitating the yellow dinitrophenylhydrazone of acetophenone when its preparation was repeated; this made it possible to increase the yield to 0.53-0.54 g. For purification 1.0 g of the yellow substance was recrystallized from a mixture of 60 ml alcohol and 12 ml ethyl acetate. 0.84 g of substance was obtained as glistening golden-yellow scales. M.p. 147-147.5° (cor.).

b) 1.0 g of dinitrophenylhydrazine and 0.7 ml of acetophenone were dissolved in 10 ml of pyridine and the solution was boiled for 25 minutes. Red needlelike crystals (0.82 g) were obtained when the solution was cooled. 10 ml of water was added dropwise to the pyridine filtrate and the thus obtained brown-yellow precipitate (0.32 g) was filtered. For purification the precipitate was recrystallized several times from pyridine (3 ml) with animal charcoal, water being added to the pyridine filtrate. However, this method gave a not completely pure brown-yellow product with m.p. 144-146°.

Transformation of the Yellow Isomer of Acetophenone Dinitrophenylhydrazone into the Red Isomer

The yellow dinitrophenylhydrazone of acetophenone was heated in a test tube for 5 minutes at 240°. The substance turned red and on cooling congealed to a red crystalline mass, which now melted at 233-235°, and after recrystallization from pyridine at 244-246° (cor.) with slight decomposition. The yellow dinitrophenylhydrazone of acetophenone was dissolved in glacial acetic acid. After boiling the solution and then cooling, the red dinitrophenylhydrazone of acetophenone was obtained as a crystalline product. The same transformation takes place in concentrated sulfuric acid solution at room temperature in 1-2 days. The yellow dinitrophenylhydrazone of acetophenone was dissolved in alcoholic alkali solution to give a cherry-red solution. Acidification of the solution gave the red dinitrophenylhydrazone of acetophenone.



Absorption curves for the red and yellow isomers of acetophenone 2,4-dinitrophenylhydrazone. 1) Red: λ_{max} 375 mμ, ε 2.98; 2) yellow: λ_{max} 365 mμ, ε 2.58.

Analysis of the yellow isomer:

0.0962 g sub.: 0.1966 g CO_2; 0.0368 g H_2O. 0.0995 g sub: 0.2031 g CO_2; 0.0367 g H_2O. 0.0894 g sub.: 14.2 ml N_2 (19°, 775.5 mm). 0.0995 g sub.: 15.7 ml N_2 (22°, 765.6 mm). Found %: C 55.77, 55.70; H 4.28, 4.13; N 18.80, 18.93. $C_{14}H_{12}O_4N_4$. Calculated %: C 56.0; H 4.0; N 18.67

Analysis of the red isomer:

0.1016 g sub.: 0.2083 g CO_2; 0.0386 g H_2O. 0.0951 g sub.: 15.3 ml N_2 (20°, 769.5 mm). Found %: C 55.95; H 4.25; N 18.82. $C_{14}H_{12}O_4N_4$. Calculated %: C 56.0; H 4.0; N 18.67.

Ultraviolet absorption spectra of the red and yellow isomers of acetophenone 2,4-dinitrophenylhydrazone. The absorption curves were determined with the aid of a SF-II spectrophotometer. The investigated compounds were dissolved in dioxane. The thickness of the absorption layer was 0.5 cm. M 300.

The red isomer was taken at a concentration of 0.02 g/liter, i.e., its molar concentration was $0.02:300 = 0.67 \cdot 10^{-4}$ M, from which the molecular absorption coefficient, $\epsilon = D \cdot 3 \cdot 10^4$, where D is the observed optical density.

The yellow isomer was taken at a concentration of 0.04 g/liter, i.e., its molar concentration was $0.04:300 = 1.33 \cdot 10^{-4}$ M., from which for it $\epsilon = D \cdot 1.5 \cdot 10^4$.

Our obtained results are given in the figure.

SUMMARY

1. In contrast to the oximes, the hydrazones of unsymmetrical ketones fail to exhibit geometric isomerism. With other conditions constant, rotation around the C=N double bond is more difficult for the oximes than it is for the hydrazones. This is explained by the difference in the influence of the OH (for oximes) and NH_2 (for hydrazones) groups on the "resonance" of the C=N double bond. The NH_2 group has the more mobile π-electrons, its induction effect is greater, and consequently it exerts a strong influence on the C=N double bond in the sense of lowering its double bond nature.

The "resonance" of the C=N double bond in phenylhydrazones is increased if nitro groups are introduced into the phenyl radical, especially in the ortho- and para-positions, inasmuch as the latter draw the π-electrons of the NH group and in that way oppose their displacement toward the C=N group. This is confirmed by the appearance of geometric isomerism for a number of 2,4-dinitrophenylhydrazones of aldehydes and unsymmetrical ketones.

2. In all cases the presence of the methyl group makes closure of the pyrazolone ring more difficult than when phenyl is present. This difference is especially noticeable in the formation of 1-(2',4'-dinitrophenyl)-3-methyl-5-pyrazolone and 1-(2',4'-dinitrophenyl)-3-phenyl-5-pyrazolone. Two nitro groups (in the 2- and 4-positions of the phenyl radical) raise the "resonance" of the C=N double bond to such an extent in the phenylhydrazones of acetoacetic and benzoylacetic esters that in the formation of pyrazolone rings from them the same rule holds true as was observed in the formation of isoxazolone rings from the corresponding oximes; in the presence of methyl the stable hydrazone is formed, which is transformed into the pyrazolone with exceedingly great difficulty; in the presence of phenyl the pyrazolone is formed immediately.

3. The similarity of the nitrated phenylmethylpyrazolones and diphenylpyrazolones to the isoxazolones further consists in that the pyrazolones, containing 2 or 3 nitro groups in the phenyl radical, are readily hydrolyzed to the corresponding hydrazones of acetone or of acetophenone. Similar hydrolysis of phenylisoxazolone gives the oxime of acetophenone.

The transition from 1-(2',4'-dinitrophenyl)-3-phenyl-5-pyrazolone to the 2,4-dinitrophenylhydrazone of acetophenone permits ascribing to the latter the syn-methyl configuration. The postulation of a definite molecular arrangement in space of the 2,4-dinitrophenylhydrazone of acetophenone finds support in the fact that we were able to obtain the latter in the form of two isomers. The properties and transformations of these isomers reveal that they are syn-anti-stereoisomers.

The discovery in recent years of new dinitrophenylhydrazone stereoisomers tends to support the above presented theories.

LITERATURE CITED

[1] Meisenheimer, Weibezahn, Ber., 54, 3195 (1921).

[2] Kohler, J. Am. Chem. Soc., 46, 1733 (1924).

[3] Beckmann, Ber., 20, 1509, 2581, 2583 (1887).

[4] Straus, Berkow, Ann., 401, 141 (1913).

[5] Graziano, Gazz., 45, II, 393 (1915).

[6] Schröter, Ber., 44, 1204 (1911).

[7] Collet, Bull. Soc. Chem., (3), 27, 540 (1902).

[8] Korten, Scholl, Ber., 34, 1904 (1901).

[9] Finze, Gazz., 42, II, 359 (1912).

[10] Werner, Piguet, Ber., 37, 4307 (1904).

[11] Kohler, J. Am. Chem. Soc., 31, 650 (1909).

[12] Hantzsch, Ber., 24, 4018 (1891).

[13] Auwers and Jordan, Ber., 57, 800 (1924).

[14] Meisenheimer, Meis, Ber., 57, 291 (1924).

[15] Meyenburg, Ber., 26, 1658 (1893).

[16] Huntress, Walter, J. Am. Chem. Soc., 70, 3702 (1948).

[17] V. Meyer and W. Scharwin, Ber., 30, 1940(1897).

[18] Kissman, Williams, J. Am. Chem. Soc., 72, 5323 (1950).

[19] Hantzsch, Ber., 25, 2164 (1892).

[20] Abegg, Ber., 32, 291 (1899).

[21] A. E. Porai-Koshits and N. V. Khromov, J. Gen. Chem., 10, 557 (1940).

[22] N. V. Khromov, J. Gen. Chem., 20, 1858 (1950).*

[23] Felkin, Comptes rend., 227, 510 (1948).

[24] Volhard, Ann., 296, 4 (1897).

[25] Piutti, Gazz., 18, 457 (1888).

[26] Huge, Ber., 32, 1810 (1899).

[27] Bredereck, Ber., 65, 1933 (1932).

[28] Bredereck, Fritzsche, Ber., 70, 802 (1937).

[29] Allen, Richmond, J. Org. Chem., 2, 222 (1937).

[30] Veibel, Acta chemica Scandinavica, I, No. 1, 54 (1947).

[31] Hantzsch, Ber., 24, 495 (1891).

[32] A. I. Kiprianov and I. K. Ushenko, Bull. Acad. Sci. USSR, Div. Chem. Sci., 1950, No. 5, 499.

[33] A. N. Terenin, Photochemistry of Dyes, Acad. Sci. USSR Press, Moscow-Leningrad, 24 (1947).

[34] Theilacker, Ber., 82, 190 (1949).

[35] Dirscherl, Nahm, Ber., 74, 448 (1940).

[36] Bauer, Strauss, Ber., 65, 308 (1932).

[37] Altschul, Ber., 25, 1853 (1892).

[38] Purgotti, Gazz., 24, I, 569 (1894); Curtius, Dedichen, J. prak. Chem., (2), 50, 267 (1894).

[39] Purgotti, Gazz., 24, I, 580 (1894).

[40] Knorr, Klotz, Ber., 20, 2546 (1887).

[41] Michaelis, Willert, Ann., 358, 177 (1908).

Received April 12, 1954

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* See Consultants Bureau Translation, page 1923.

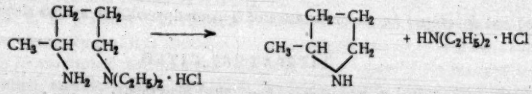
MOBILITY OF THE DIETHYLAMINO GROUP

II. SYNTHESIS OF α-METHYLPYRROLIDINE

V. I. Stavrovskaya

Several methods are described in the literature for the preparation of α-methylpyrrolidine [1-3], the starting materials usually used in the synthesis being five-membered nitrogen compounds.

α-Methylpyrrolidine was obtained by us from 1-diethylamino-4-aminopentane in 60% yield by heating the monohydrochloride in a sealed tube for 20 hours at 180-185°. The reaction proceeds with the cleavage of diethylamine hydrochloride in accord with the scheme



The monohydrochloride required for the reaction was formed by charging equimolecular amounts of dihydrochloride and diamine base into the tube. Under these conditions the monohydrochloride of 1-diethylamino-4-benzylaminopentane gave N-benzyl-α-methylpyrrolidine in 67% yield. We also obtained the latter compound by the direct reaction of benzyl chloride with α-methylpyrrolidine. The hydrochlorides of N-benzyl-α-methylpyrrolidine, obtained by the above indicated methods, failed to show a mixed melting point depression.

EXPERIMENTAL

α-Methylpyrrolidine

A mixture of 1-diethylamino-4-aminopentane (9.5 g) and its dihydrochloride (13.8 g) was heated in a sealed tube for 20 hours at 180-185°. On conclusion of heating the tube contents were a brown friable crystalline mass saturated with a brown mobile liquid. The reaction mass was treated with a 40% sodium hydroxide solution and extracted with ether. The ether extract was dried over potash. After the ether and diethylamine, formed in the reaction, were removed by distillation the residue was dried over solid potassium hydroxide, after which it was subjected to fractional distillation. The fraction, collected at 94-98° (734 mm), is α-methylpyrrolidine. Yield 6.1 g (60%).

1-Diethylamino-4-benzylaminopentane. A mixture of benzyl chloride (12.6 g) and 1-diethylamino-4-aminopentane (32 g) was heated under reflux for 6 hours on the boiling water bath. After cooling, the viscous reddish-orange liquid was treated with 10% sodium hydroxide solution and then extracted with ether. The ether extract was washed with water and then dried over potash. After the ether and unreacted 1-diethylamino-4-aminopentane were removed by distillation the residue was vacuum distilled, the fraction with b.p. 134-135° at 4 mm* being collected. Yield 12.5 g (50%).

The base 1-diethylamino-4-benzylaminopentane is a colorless mobile liquid.

Found %: N 11.40, 11.58. $C_{16}H_{28}N_2$. Calculated %: N 11.29.

N-Benzyl-α-methylpyrrolidine

a) A mixture of 1-diethylamino-4-benzylaminopentane (5 g) and its dihydrochloride (6.5 g) was heated in a sealed tube for 11 hours at 185-190°. After cooling, the tube contents were a light brown crystalline mass with a small amount of liquid. The reaction mixture was treated with a 40% sodium hydroxide solution and then extracted with ether. The ether extract was dried over potash. After the ether was removed by distillation there remained 5.7 g of mobile yellow liquid, which was vacuum distilled, b.p. 84° at 5 mm. Yield 4.7 g (67%). The addition of alcoholic HCl to the base gave the hydrochloride, which was recrystallized from acetone or from alcohol and ether. Plates, m.p. 172-173°. The white hydrochloride is readily soluble in water.

* In the literature this compound is given b.p. 187-189° at 25 mm [4].

4.180 mg sub.: 0.284 ml N_2 (20°, 755 mm). 4.639 mg sub.: 0.274 ml N_2 (21°, 755 ml). Found %: N 6.83, 6.81. $C_{12}H_{18}NCl$. Calculated %: N 6.62.

The hydrochloride was converted into the base, which distilled at 101° at 10 mm. The base is a colorless mobile liquid, readily soluble in alcohol, ether, benzene, dilute acids, and insoluble in water.

6.210 mg sub.: 0.441 ml N_2 (20°, 761 mm). 2.595 mg sub.: 0.186 ml N_2 (19°, 756 mm). Found %: N 8.28, 8.33. $C_{12}H_{17}N$. Calculated %: N 8.00.

b) Benzyl chloride (2.5 g) and α-methylpyrrolidine (2 g) were poured together with strong heat evolution being observed. The flask with reaction liquid was heated on the boiling water bath for 6 hours. After cooling, the viscous reaction mass was treated with a 10% sodium hydroxide solution and then extracted with ether. The ether extract was dried over potash. After the ether was removed by distillation there remained 2.8 g of mobile liquid, which was vacuum distilled, b.p. 97-98° at 9-10 mm. Yield 2.1 g (60%). The white hydrochloride had m.p. 172-173°. The mixed melting point with the hydrochloride of N-benzyl-α-methylpyrrolidine, obtained by the preceding method, failed to be depressed.

SUMMARY

A new method was developed for the preparation of α-methylpyrrolidine and its N-benzyl derivative.

LITERATURE CITED

[1] A. Ladenburg, M. Mugdan, O. Brzostovicz, Ann., 279, 354 (1894).

[2] Maskerelli, Testoni, Gazz., 33, 11, 315 (1903).

[3] G. Fenner, J. Tafel, Ber., 31, 909 (1898).

[4] T. S. Work, J. Chem. Soc., 1942, 426.

Received May 26, 1954

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INVESTIGATIONS IN THE FIELD OF TAUTOMERIC COMPOUNDS

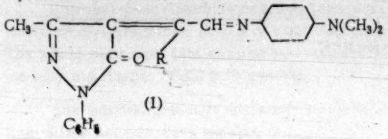
XVIII. REACTION OF ISOPROPYLIDENE- AND ARYLETHYLIDENE-PHENYLMETHYLPYRAZOLONES WITH NITROSODIMETHYLANILINE AND NITROUS ACID

A. E. Porai-Koshits* and M. S. Dinaburg

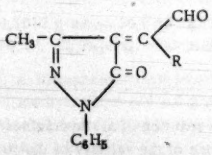
In previous communications [1, 2] it was shown that the substances obtained in the condensation of phenylmethylpyrazolone with methyl ketones readily react with aldehydes and diazo compounds, and consequently they possess an extremely reactive methylene group.

It was revealed that they are also capable of reacting with nitroso compounds, in particular, with nitrosodimethylaniline. In contrast to the majority of compounds with mobile hydrogen atoms, the investigated substances enter into this reaction so vigorously that it is necessary to resort to good cooling in order to avert secondary reactions. However, it should be mentioned that even when this condition is observed the reaction is always accompanied by considerable tar formation, especially in the case of the less stable starting compound – isopropylidene-phenylmethylpyrazolone. In the condensation of the latter with nitrosodimethylaniline the yield of reaction product fails to exceed 8-15%.

The reaction of methylene derivatives with nitrosodimethylaniline results in the formation of deeply colored crystalline substances, the structure of which can be represented by the general formula (I).



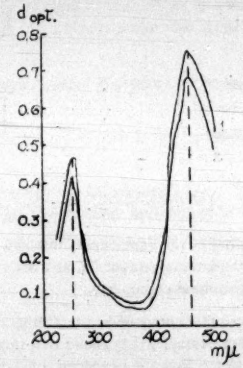
(I)



(II)

Like all azomethine compounds, these substances are cleaved by mineral acids with the formation of the corresponding aldehydes (II).

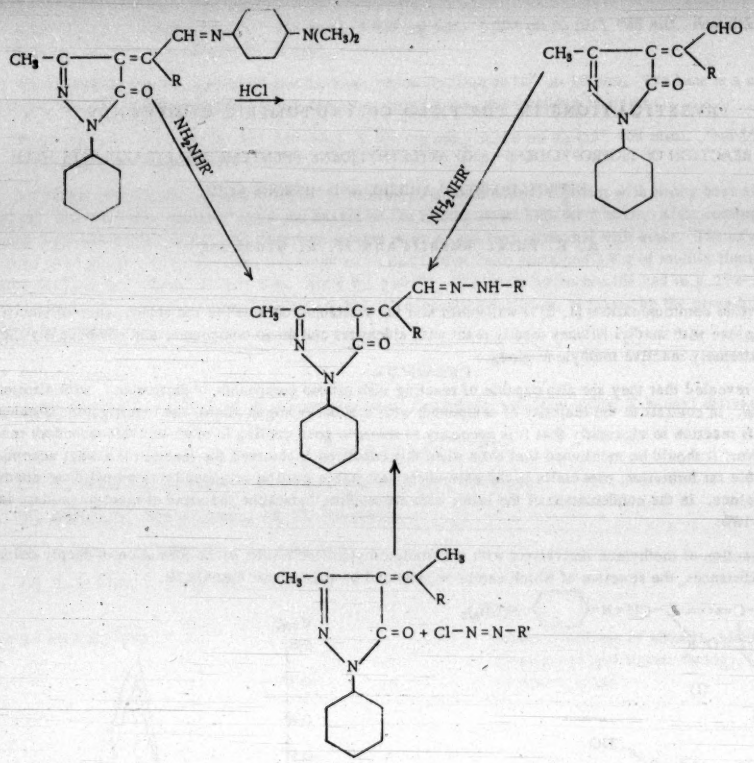
We were able to isolate the aldehyde in the free state only in the case of the acetophenone derivative ($R = C_6H_5$) (III). In two other cases – where $R = CH_3$ (IV) and $R = m\text{-}NO_2C_6H_4$ – the aldehydes were identified as the oximes, semicarbazones, and hydrazones. The latter, in particular, can be obtained both from the aldehydes, and directly from the azomethine compounds by reacting them with arylhydrazines. The properties of the hydrazones, the elementary analysis data, the absence of mixed melting point depression, the comparative absorption spectra curves, etc., demonstrate the fact that they are identical with the products obtained in the azo-coupling of the original methylene derivatives with diazo compounds.



1) Phenylhydrazone of phenylmethylpyrazolonylidene-acetaldehyde; 2) 4-(α-phenyl-β-phenylazo)ethylidene-phenylmethylpyrazolone.

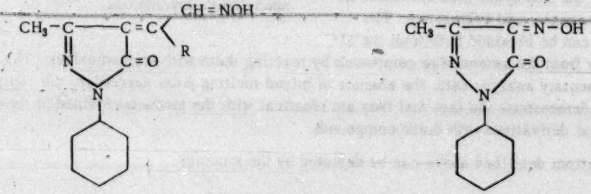
The transformations described above can be depicted by the scheme:

* Deceased.



The identity of the compounds, obtained by direct azo-coupling and by the reaction of arylhydrazines with aldehydes or azomethine compounds, as a result, is sufficiently convincing evidence of the validity of the structures assigned above to these compounds.

It is known that compounds, containing mobile hydrogen atoms, in certain cases are capable of reacting with nitrous acid. For example, it is known that isonitrosoacetophenone can be obtained by reacting amyl nitrite with acetophenone in the presence of sodium ethylate [3]. Trinitrotoluene and a number of other compounds react under analogous conditions. However, as a rule, the mentioned compounds are incapable of reacting with aqueous nitrous acid solutions. It was revealed that the studied phenylmethylpyrazolones react with great ease also with aqueous nitrous acid solutions, in which connection the 4-α-phenylethylidene- and 4-α-(m-nitrophenyl)ethylidenephenylmethylpyrazolones form the corresponding isonitroso compounds (VI) and (VII).



(VI-VII) (VIII)

R = C_6H_5 (VI) or R = m-$C_6H_4NO_2$ (VII)

The structure of the latter were proved by their synthesis from phenylmethylpyrazolone and isonitrosoacetopenone.

On the other hand, the isonitroso compounds proved to be identical to the corresponding oximes, which were obtained by the action of hydroxylamine on aldehydes or directly on the azomethine compounds.

As regards the reaction of nitrous acid with isopropylidene phenylmethylpyrazolone, in this case the reaction is different from that of the above described compounds. Instead of the expected isonitroso compound being formed, the reaction that takes place is displacement of the ketone radical from the molecule to yield the well-known isonitrosophenylmethylpyrazolone (VIII).

EXPERIMENTAL

I. Reaction of Methylene Derivatives with p-Nitrosodimethylaniline

[(Phenyl-phenylmethylpyrazolonylidene)ethylidene]-dimethyl-p-phenylenediamine. 11 g of phenylethylidene-phenylmethylpyrazolone and 6 g of p-nitrosodimethylaniline were ground in a mortar, transferred to a beaker, and with cooling stirred with 70 ml of ethyl alcohol. A thick crystalline mass was obtained almost immediately. After 2 hours the crystals were filtered, washed with boiling alcohol (30 ml), and dried. Yield 13.0 g (68%). The mass of fine crystals was boiled with 20-30 ml of alcohol, filtered from the brown liquid, and dried. Bright bronze green needles, m.p. 180-181°.

For purification the crystals were dissolved in boiling acetone and an equal volume of hot water (50°) was carefully added. The product separated as bright green glistening needles, m.p. 181°.

0.1143 g sub.: 0.3203 g CO_2; 0.0629 g H_2O. 0.1103 g sub.: 0.3087 g CO_2; 0.0603 g H_2O. 0.0850 g sub.: 10.1 ml N_2 (14°, 752 mm). 0.0936 g sub.: 11.2 ml N_2 (14°, 752 mm). Found %: C 76.41, 76.29; H 6.11, 6.06; N 13.85, 14.06. $C_{25}H_{24}ON_4$. Calculated %: C 76.47; H 5.88; N 13.72.

[(Methyl-phenylmethylpyrazolonylidene)ethylidene]-dimethyl-p-phenylenediamine. 1.06 g of isopropylidene-phenylmethylpyrazolone, 0.75 g of p-nitrosodimethylaniline and 10 ml of alcohol were stirred in a beaker at 8-10°. The whole mass went into solution very quickly, and on rubbing with a rod a bronze green precipitate separated from the ruby red liquid. Yield 0.12 g (~7%).

The solution gradually darkened to a dark brown without further separation of product. Two recrystallizations from dilute acetone gave needles, m.p. 184-185°.

0.1017 g sub.: 14.1 ml N_2 (16°, 758 mm). 0.0859 g sub.: 12.0 ml N_2 (16°, 758 mm). Found %: N 16.33, 16.50. $C_{21}H_{22}ON_4$. Calculated %: N 16.20.

[(m-Nitrophenyl-phenylmethylpyrazolonylidene)ethylidene]-dimethyl-p-phenylenediamine. 2.25 g of p-nitrosodimethylaniline and 4.8 g of m-nitrophenylethylidenephenylmethylpyrazolone were mixed with 100 ml of ethyl alcohol and allowed to stand at −5°. After 4 hours the copious crystalline deposit was filtered. Yield 6.1 g (90%). M.p. 185°.

The substance is readily soluble in most organic solvents. From aqueous acetone or benzene-alcohol mixture it crystallizes with extremely large losses as microscopic needles, m.p. 185°.

0.1731 g sub.: 0.4371 g CO_2; 0.0709 g H_2O. Found %: C 68.78; H 5.07. $C_{26}H_{23}ON_5$. Calculated %: C 68.85; H 5.07.

Phenyl-phenylmethylpyrazolonylideneacetaldehyde. 4.08 g of the azomethine (III) was dissolved in 40 ml of dry acetone and to the solution with good stirring was added 2.0 ml of concentrated hydrochloric acid. The color of the solution changed from reddish-violet to orange-yellow and a dark brown oil deposited on the sides of the beaker. The acetone solution was decanted and the oil was washed with two portions (20 ml each) of dry acetone; the wash liquors were combined with the main solution and water was added dropwise until crystallization began. After two hours the product was filtered, washed with dilute acetone, and dried. Yield 1.77 g (61%).

An almost colorless oil remained on the sides of the beaker after washing with acetone. The oil was extracted with benzene, the solution dried over sodium sulfate, filtered, and then boiled with phthalic anhydride. After 3 hours the yellow phthaloyl derivative of dimethyl-p-phenylenediamine separated; m.p. 167°. No depression of the melting point was observed when mixed with the preparation obtained by the literature method.

0.2114 g sub.: 0.5524 g CO_2; 0.0978 g H_2O. Found %: C 77.73; H 5.14. $C_{17}H_{14}ON_2$. Calculated %: C 77.86; H 5.34.

Phenylhydrazone of phenyl-phenylmethylpyrazolonylideneacetaldehyde. a) 0.4 g of the azomethine (III) was dissolved in the cold in 10 ml of glacial acetic acid and to the solution was added 0.11 g of phenylhydrazine and 2 ml of glacial acetic acid. The color of the solution immediately changed from bluish violet to ruby red; after 1-2 minutes the solution became completely clear. 5 ml of warm water was added dropwise to the solution. Crystallization began after several minutes. After 1 hour the product was filtered, washed with dilute alcohol, and dried. Yield 0.21 g (55%). Ruby red leaflets from alcohol, m.p. 118°. No depression of the melting point was observed when mixed with phenylazophenylethylidenephenylmethylpyrazolone.

b) 0.29 g of the aldehyde was dissolved in 10 ml of 70% acetic acid and 0.11 g of phenylhydrazine in 1-2 ml of acetic acid was added. After several minutes the solution acquired a deep red color and the crystalline reaction product began to precipitate. Yield 0.3 g (79%). M.p. 118°.

p-Nitrophenylhydrazone of phenyl-phenylmethylpyrazolonylideneacetaldehyde. 0.29 g of the aldehyde (II) and 0.16 g of p-nitrophenylhydrazine were brought up to the boil in 5 ml of 75% acetic acid. The reaction product began to crystallize immediately. After 1 hour the product was filtered, washed with alcohol, and dried. Yield 0.26 g (61.2%). M.p. 235-236°.

Rapid crystallization from glacial acetic acid gave brown prisms, m.p. 235-236°, while slow cooling gave long, dark green needles. No depression of the melting point was observed when mixed with the corresponding azo compound.

0.1441 g sub.: 0.3572 g CO_2; 0.0630 g H_2O. 0.1459 g sub.: 20.8 ml N_2 (17°, 760 mm). Found %: C 67.65; H 4.85; N 16.67. $C_{24}H_{19}O_3N_5$. Calculated %: C 67.76; H 4.47; N 16.46.

Semicarbazone of phenyl-phenylmethylpyrazolonylideneacetaldehyde. 0.5 g of the aldehyde (II) was mixed with 0.18 g of semicarbazide hydrochloride, dissolved in 10 ml of ethyl alcohol and neutralized with soda. The mixture was heated up to the boil, at which point the crystalline product began to separate. Fine red crystalline powder. Yield 0.51 g Tiny red prisms from acetic acid, m.p. 227-227.5°.

p-Nitrophenylhydrazone of m-nitrophenyl-phenylmethylpyrazolonylideneacetaldehyde. 1.27 g of the azomethine (V) and 0.4 g of p-nitrophenylhydrazine were brought up to the boil in 20 ml of glacial acetic acid. After 5-10 minutes a brownish-green crystalline precipitate began to separate. Yield 0.7 g (54.0%). Needles from aqueous pyridine, m.p. 250-251° (decomposition). No depression of the melting point was observed when mixed with the product obtained by the azo-coupling of m-nitrophenylethylidenephenylmethylpyrazolone with p-nitrophenyldiazonium chloride.

Phenylhydrazone of methyl-phenylmethylpyrazolonylideneacetaldehyde. 0.35 g of the azomethine (IV) and 0.12 g of phenylhydrazine were brought up to the boil in 5 ml of glacial acetic acid. After 1-2 minutes the solution became ruby red. On cooling there was obtained 0.22 g of substance. Bright red scales from glacial acetic acid, m.p. 173-174°. No depression of the melting point was observed when mixed with phenylazo-4-isopropylidenephenylmethylpyrazolone.

Oxime of phenyl-phenylmethylpyrazolonylideneacetaldehyde. 2.9 g of the aldehyde (II) was dissolved in 30 ml of alcohol and to it was added an alcohol solution of 1.0 g of hydroxylamine hydrochloride that had been neutralized with soda. The solution became red in color. 5 ml of water was added, the obtained precipitate was filtered, washed with alcohol, and dried. Yield 2.0 g (65%). Bright red prisms from methyl alcohol, m.p. 208°.

0.1802 g sub.: 0.4677 g CO_2. 0.0844 g H_2O. 0.1467 g sub.: 17.4 ml N_2 (16°, 758 mm). Found %: C 70.77; H 5.20; N 13.95. $C_{18}H_{15}O_2N_3$. Calculated %: C 70.84; H 4.91; N 13.77.

Oxime of m-nitrophenyl-phenylmethylpyrazolonylideneacetaldehyde. 0.2 g of the azomethine (V) was dissolved in 5 ml of glacial acetic acid and a solution of 0.05 g of hydroxylamine hydrochloride in 2 ml of glacial acetic acid was added. After 15-20 minutes the obtained precipitate was filtered and washed with dilute acetic acid. Yield 0.19 g (60%). M.p. 235-236°.

II. Reaction of Methylene Derivatives with Nitrous Acid

4-(α-Phenyl-β-isonitrosoethylidene)phenylmethylpyrazolone. 2.76 g of 4-α-phenylethylidenephenylmethylpyrazolone was dissolved in 15 ml of acetone. The addition of 2.0 ml of concentrated hydrochloric acid resulted in almost complete decolorization of the solution. With cooling a solution of 0.69 g of nitrite in 2 ml of water was added dropwise. Immediately the red crystalline reaction product in admixture with sodium chloride was obtained. The precipitate was filtered, and washed with dilute acetone, water, and alcohol. Yield 2.5 g (82%). M.p. 205°. Tiny bright red prisms from either ethyl or methyl alcohol, m.p. 208°.

The substance is soluble in 10-15% sodium hydroxide solution; when treated with an excess of alkali the crystalline sodium salt is obtained, crystallizing from water as brown platelets.

0.1454 g sub.: 0.3771 g CO_2; 0.0657 g H_2O. 0.1522 g sub.: 0.3962 g CO_2; 0.0679 g H_2O. 0.1056 g sub.: 12.6 ml N_2 (22°, 770 mm). Found %: C 70.74, 70.98; H 5.01, 4.95; N 14.05. $C_{18}H_{15}O_2N_3$. Calculated %: C 70.84; H 4.91; N 13.77.

Condensation of isonitrosoacetophenone with phenylmethylpyrazolone. a) 2.48 g of phenylmethylpyrazolone, 3.0 g of isonitrosoacetophenone and 15 ml of ethyl alcohol were heated under reflux. After 1 hour the solution turned dark red. The solution was cooled and about 15 ml of water was added dropwise. After 3 hours the obtained precipitate was filtered. Bright red prisms, m.p. 205-206°. Yield 0.94 g. An oil was obtained on increasing the amount of water. The oil was dissolved in 50 ml of acetone and 15 ml of water was added. After 1 hour the crystalline product was filtered. Yield 1.15 g. M.p. 204-206°. Total yield 2.09 g (30%).

b) 1.74 g of phenylmethylpyrazolone, 1.5 g of isonitrosoacetophenone and 10 ml of methyl alcohol were allowed to stand at room temperature. After 72 hours the obtained precipitate was filtered and washed with alcohol. Yield 1.6 g (50.8%). Prisms from alcohol, m.p. 208°. No depression of the melting point was observed when mixed with the substance obtained by the nitrosation of the methylene derivative and with the oxime of phenyl-phenylmethylpyrazolonylideneacetaldehyde.

4-[(α-m-Nitrophenyl-β-isonitroso)ethylidene]phenylmethylpyrazolone. 4.9 g of m-nitrophenylethylidenephenylmethylpyrazolone was mixed with 25 ml of acetone and 5.5 ml of concentrated hydrochloride, after which a 30% sodium nitrite solution was added to positive reaction with starch iodide paper. The obtained precipitate was filtered and washed with dilute acetone. Yield 4.45 g (84%). Red plates from aqueous pyridine, m.p. 235-236° (decomposition). The substance is soluble in 0.1 N sodium hydroxide solution with the formation of dark red solutions. The substance failed to give a depression of the melting point when mixed with the oxime of m-nitrophenyl-phenylmethylpyrazolonylideneacetaldehyde.

0.1243 g sub.: 0.2800 g CO_2; 0.0443 g H_2O. 0.1344 g sub.: 18.7 ml N_2 (20°, 758 mm). Found %: C 61.49; H 3.98; N 16.17. $C_{18}H_{14}O_4N_5$. Calculated %: C 61.71; H 4.00; N 16.00.

Reaction of nitrous acid with isopropylidenephenylmethylpyrazolone. 2.12 g of isopropylidenephenylmethylpyrazolone was dissolved in 15 ml of ethyl alcohol and 2 ml of concentrated hydrochloric acid was added. To the solution was added a concentrated solution of 0.69 g of sodium nitrite. After 2 hours the copious crystalline precipitate was filtered, washed with alcohol, and recrystallized from benzene-petroleum ether mixture. Yellow-orange needles, m.p. 157°. Soluble in alkalis with an intense blue coloration. No depression of the melting point was observed when the substance was mixed with the isonitrosophenylmethylpyrazolone prepared according to the literature.

SUMMARY

1. The condensation products of phenylmethylpyrazolone with methyl ketones react with nitroso compounds and with nitrous acid to give the corresponding azomethine and isonitroso compounds. An exception is isopropylidenephenylmethylpyrazolone, which suffers cleavage under the influence of nitrous acid.

2. The identity of the products obtained by the reaction of azomethine compounds or aldehydes with arylhydrazines and hydroxylamine with the products obtained by the azo coupling and nitrosation of the original methylene derivatives is convincing proof of the validity of the established structure.

LITERATURE CITED

[1] A. E. Porai-Koshits and M. S. Dinaburg, J. Gen Chem., 24, 1221 (1954).

[2] A. E. Porai-Koshits and M. S. Dinaburg, J. Gen. Chem., 24, 2208 (1954).

[3] Claissen, Manasse, Ber., 20, 2194 (1887); Claisen, Ber., 20, 656 (1887).

Received April 30, 1954

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INVESTIGATION OF ACONITE ALKALOIDS

II. THE ALKALOIDS OF DELPHINIUM DICTYOCARPUM DC

A. D. Kuzovkov, P. S. Massagetov, and M. S. Rabinovich

The material used for the isolation and chemical study of alkaloids was the above-ground portion of the reticulate bearing larkspur (Delphinium dictyocarpum DC.), collected in the northwest regions of Tarbagataya at the flowering stage. From this material a total of 0.4% of noncrystalline alkaloids was isolated, from which 0.1% of crystalline perchlorate was obtained, m.p. 187-189° (from 70% alcohol), $[\alpha]_D$ + 27.5°. The base, isolated from the perchlorate, is an amorphous glassy substance with m.p. about 130°, $[\alpha]_D$ +48.1°. As can be seen from Table 1, further studies of the alkaloid revealed it to be identical with methyllycaconitine. In addition, the constants of the alkaloid obtained by us, and the nature and constants of its hydrolysis products, in no way differ from those for the alkaloids delartine and delsemidine, which can also be seen from Table 1. Then we made a direct

TABLE 1

Constants of the Alkaloids and of Their Hydrolysis Products

Constants of the substances		Alkaloid from D. dictyocarpum	Methyllycaconatine	Delartine [5]	Delsemidine [3]
Alkaloid					
Base	Melting point	About 130°	128°	110-130°	122-130
	$[\alpha]_D$	+48.1	+49.1	+45.1	+ 46.6
Perchlorate	Melting point	188-189	–	188-190	194-195
	$[\alpha]_D$	+27.5	–	+ 25.08	+25.4
Hydroiodide	Melting point	196-197	201°	–	199-202
	$[\alpha]_D$	+ 32.8	+ 31.2	–	–
Product of Hydrolysis					
Acid		Methylsuccinylanthranilic		Nature not determined	Methylsuccinylanthranilic
Melting point		161-163°	155-156°	160-164°	163-164°
Amino Alcohol					
Base	Melting point	143	143	142-145	140
	$[\alpha]_D$	+52.6	+53.2	+53.3	+51.5
Hydrochloride	Melting point	160-161	152	159-162	165
	$[\alpha]_D$	+14.7	–	–	+13.8
Hydrobromide	Melting point	171-172	171.5-172	167-169	185
	$[\alpha]_D$	+14.7	–	–	+14

comparison of the amino alcohols available to us from the alkaloids delartine, delsemidine, and from the alkaloid isolated from Delphinium dictyocarpum. All of these amino alcohols crystallized from 70% alcohol as slender needles, containing solvent of crystallization. When their melting points were determined in an open capillary the amino alcohols underwent dehydration and partial decomposition, in which connection a wide melting range which strongly depended on the rate of heating was observed. Better results were obtained when the melting

points of these amino alcohols were determined in a vacuum: the melting point was raised by 8-10° and was independent of the rate of heating; the substance failed to decompose (on cooling it again became crystalline). The melting points obtained by us for the amino alcohols and their mixtures in a vacuum are given in Table 2.

TABLE 2

Melting Points of the Amino Alcohols and Their Mixtures

Amino alcohol from			Mixture		
Alkaloid isolated from D. Dictyocarpum (I)	Delartine (II)	Delsemidine (delsine) (III)	I and II	I and III	II and III
150-151	147-149°	150-152°	150-151°	150-152°	150-152°

The formula $C_{37}H_{43}O_{10}N_2$ [1] has been proposed for methyllycaconitine, for delartine $C_{36}H_{52}O_{11}N_2$ [2], and for delsemidine $C_{37}H_{50}O_{10}N_2$ [3], while the formulas proposed for the corresponding alcohols are $C_{25}H_{39}O_7N$ [1], $C_{26}H_{43}O_7N$ [2], and $C_{25}H_{41}O_7N$ [3]. However, the difference in the empirical formulas is apparently not due to a difference in the analytical results, obtained by the different authors, but is due to the fact that for such a large molecule it is possible to assign several empirical formulas. The formulas of S. Yu. Yunusov and N. K. Abubakirov [3] for delsemidine ($C_{37}H_{50}O_{10}N_2$) and the amino alcohol from this alkaloid ($C_{25}H_{41}O_7N$) agree best of all with the analytical results of other authors; consequently, it appears to us that these formulas should be given preference over the others. Table 3 illustrates the proximity of these formulas with the analytical results of Rabinovich and Konovalova [2] and of Goodson [1].

TABLE 3

Analysis Results for Alkaloid and Amino Alcohol

Substance	Calculated %	Found %
Alkaloid		
Perchlorate $C_{37}H_{50}O_{10}N_2 \cdot HClO_4 \cdot 1.5H_2O$	C 55.0 H 6.7 Cl 4.53	C 54.5, 54.7 [2] H 6.8, 7.0 Cl 4.32, 4.47
Hydroiodide $C_{37}H_{50}O_{10}N_2 \cdot HI$	C 54.7 H 6.3 N 3.5 4OCH_3 15.3 I 15.7	C 54.6 [1] H 6.5 N 3.8 4OCH_3 15.9 I 14.9
Amino alcohol		
Base $C_{25}H_{41}O_7N \cdot H_2O$	C 61.8 H 8.93 N 2.88 4OH 14.01 4 OCH_3 25.56	C 62.87, 62.66 [2] H 8.88, 8.77 N 3.12, 3.02 4OH 13.62, 13.54 4OCH_3 24.99, 24.74
$C_{25}H_{41}O_7N$ (dry)	C 64.3 H 8.7 N 3.0 4 OCH_3 26.8	C 64.3 [1] H 8.7 N 3.3 4 OCH_3 26.6
Hydrochloride $C_{25}H_{41}O_7N \cdot HCl$	Cl 7.03	Cl 7.05, 6.77 [2]
Hydroiodide $C_{25}H_{41}O_7N \cdot HI$	I 21.31	I 21.0, 20.88 [2]

As a result, the postulation [3] that delartine, delsemidine, and methyllycaconitine are one and the same substance, was confirmed.

It appears to us that in the future the alkaloid should be named methyllycaconitine, while the amino alcohol should be called lycoctonine, inasmuch as these names were introduced into the chemical literature before the others and consequently are more deeply rooted.

EXPERIMENTAL

Isolation of Alkaloids from the Above-ground Parts of Delphinium Dictyocarpum*

The alkaloids were isolated in the usual manner by extraction of the ammonia moistened plants (10 kg)

* This form of Delphinium differs from the Delphinium sp. collected by one of us and investigated by M.S.Rabinovich and R. A. Konovalova [2].

with ethylene dichloride, followed by extraction of the alkaloids from the ethylene dichloride solution with 10% sulfuric acid. After alkalizing the sulfuric acid solution with 25% ammonia, the base was extracted with ether, from which 40 g of noncrystalline alkaloids was obtained. The latter were dissolved in 10% hydrochloric acid. The addition of an excess of a concentrated water solution of magnesium perchlorate gave the perchlorate of the base as an oil, which was separated by decantation from the mother liquor. On triturating with water the perchlorate was transformed into a powder, after two recrystallizations from 70% alcohol there was obtained 12 g of perchlorate: fine needles with m.p. 187-189°.

0.0960 g substance in 25 ml 70% alcohol, l = 1.89 dm, α_D +0.20°, $[\alpha]_D$ + 27.5°.

The alkaloid base was isolated from the suspension of the perchlorate in 10% aqueous ammonia by extraction with ether. After distillation of the ether and removal of traces of solvent in a vacuum an amorphous glassy substance was obtained, melting around 130°.

0.1645 g substance in 10 ml anhydrous alcohol, l = 1 dm, α_D + 0.79°, $[\alpha]_D$ + 48.1°.

The hydroiodide of the alkaloid was isolated as an oily deposit by adding alcoholic hydroiodic acid solution (obtained by dissolving freshly distilled concentrated acid in anhydrous alcohol with cooling) to an alcohol solution of the base. The deposit was separated by decantation from the mother liquor; the product crystallized when triturated with anhydrous alcohol. After three recrystallizations from alcohol, m.p. 196-197°.

0.1898 g substance in 10 ml 0.025 N alcoholic KOH, l = 1 dm, α_D +0.62°, $[\alpha]_D$ +32.8°.

Saponification of the Alkaloid from Delphinium Dictyocarpum

8 g of alkaloid base and 2.5 g of potassium hydroxide were dissolved in 50 ml of methanol and the solution was boiled for 45 minutes. After removal of the methanol in a vacuum, water was added to the residue and the obtained crystalline amino alcohol was filtered. The acidification of the alkaline mother liquor with 10% hydrochloric acid gave a crystalline acid, which after recrystallization from water melted at 161-163°. The mixed melting point with methylsuccinylanthranilic acid * gave the same temperature reading. After two recrystallizations from 70% alcohol the amino alcohol is obtained as long slender completely colorless needles. The substance, dried at 60°, when introduced into the apparatus at 120-130°, with rapid heating shrivels at 138° and melts with decomposition at 143°; the melting point in a vacuum (0.02 mm) sealed capillary is 150-151° (without decomposition). The mixed melting point with the amino alcohol from delsine was 150-152° in a vacuum, the mixed melting point with the amino alcohol from the alkaloid delartine was 150-151°.

0.0603 g substance in 3.05 ml anhydrous alcohol, l = 0.5 dm, α_D + 0.52°, $[\alpha]_D$ + 52.6°.

The hydrochloride of the amino alcohol was obtained in the usual manner. After recrystallization from a mixture of alcohol and ether and drying at 100°, the compound had m.p. 160-161°.

0.0662 g substance in 3.05 ml water, l = 0.5 dm, α_D + 0.16°, $[\alpha]_D$ + 14.7°.

The hydrobromide of the amino alcohol after recrystallization from an alcohol-ether mixture and drying at 100° had m.p. 171-172°.

0.0987 g substance in 3.15 ml water, l = 0.5 dm, α_D + 0.23°, $[\alpha]_D$ + 14.7°.

SUMMARY

1. The alkaloid methyllycaconitine was isolated from the plant Delphinium dictyocarpum DC.

2. The identity of the alkaloids delartine and delsemidine with methyllycaconitine and the identity of delsine with lycoctonine was demonstrated.

LITERATURE CITED

[1] J. A. Goodson, J. Chem. Soc., 1943, 139; W. B. Cook, O.A.Beath, J.Am.Chem.Soc., 74, 1411 (1952).

[2] M. S. Rabinovich, R.A.Konovalova, J.Gen.Chem. 19, 1387 (1949). *

[3] S. Yunusov and N. K. Abubakirov, J.Gen.Chem., 22, 1461 (1952). **

[4] S. Yunusov and N. K. Abubakirov, J.Gen.Chem. 21, 967 (1951). ***

Received April 23, 1954.

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* Methylsuccinylanthranilic acid was obtained by hydrolysis of the alkaloid delsemine [4].

** See Consultants Bureau Translation, p. 1389.

*** " " " " p.1504.

**** " " " " p.1059.

N-OXIDES OF THE QUINOXALINE SERIES

I. N-OXIDES OF QUINOXALYL-2-CARBOXYLIC ACID

A. S. Elina and O. Yu. Magidson

Newbold and Spring [1] in attempting to synthesize the N-oxides of 2-hydroxyquinoxalyl-3-carboxylic acid and quinoxalyl-2,3-dicarboxylic acid, by oxidation of these acids with hydrogen peroxide, established the fact that the presence of carboxyl and hydroxy groups in a position ortho to the quinoxalyl ring nitrogen inhibits its oxidation; there occurs, instead, decarboxylation and oxidation of the quinoxylic ring hydrocarbons at positions 2 and 3; 2,3-dihydroxyquinoxaline was obtained as the sole reaction product in both cases.

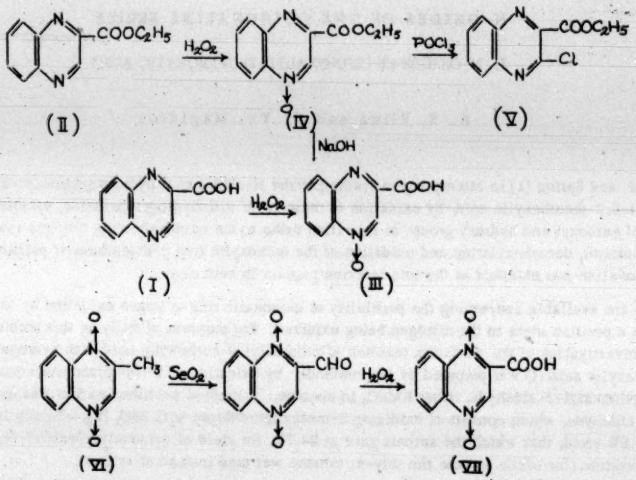
No data are available concerning the possibility of quinoxalic ring-nitrogen oxidation by the presence of carboxyl group in a position meta to the nitrogen being oxidized. For purposes of studying this problem, the authors undertook an investigation of the oxidation reaction of quinoxalyl-2-carboxylic acid with hydrogen peroxide. Quinoxalyl-2-carboxylic acid (I) was prepared by two methods: by oxidation of 2-(m-nitrostyryl)-quinoxaline, and by oxidation of quinoxalyl-2-aldehyde, using $KMnO_4$ in acetone. A method published earlier was used for synthesizing quinoxalyl-2-aldehyde, which consists of oxidizing 2-methylquinoxaline with SeO_2 [2], whereby it was possible to increase to 56.6% yield, that which the authors gave as 24.7%, for yield of quinoxalyl-2-aldehyde, by lowering the reaction temperature (for which purpose the solvent toluene was used instead of xylene).

Upon oxidizing quinoxalyl-2-carboxylic acid (I), or its ethyl ester (II), with hydrogen peroxide in glacial acetic acid medium, their mono-N-oxides were obtained. Since it was determined that the increase in H_2O_2 concentration affects positively the oxidation reaction, the 30% H_2O_2 used in the reaction was preliminarily heated in glacial acetic acid, using a specific quantity of acetic anhydride, calculated to increase the concentration to about 60%; in all probability, in this case, there proceeded only partial conversion of acetic acid into peracetic acid. Presence of the N-oxide group in the compounds obtained was established by their ability to precipitate iodine from acid solutions of KI; finally proved by reduction of the obtained mono-N-oxide of quinoxalyl-2-carboxylic acid with $Na_2S_2O_4$ in alkaline medium, with formation of initial unoxidized acid.

To determine the structure of the resulting mono-N-oxides, the ability of N-oxides of certain heterocyclic compounds to convert into chloro-derivatives when reacted with SO_2Cl_2 or $POCl_3$ was utilized. This reaction, for example, has been described for the quinoline, pyridine and pyrazine N-oxides. Quinoline and pyridine N-oxides when reacted with SO_2Cl_2 or $POCl_3$ have formed mixtures of the 2- and 4-chloro detivatives of these heterocyclic compounds [3], i.e., substitution of chlorine proceeds at ortho- and para-positions to the oxidized nitrogen. Upon heating the 1-N-oxide of 3,6-dimethylpyrazine with $POCl_3$, there resulted 2-chloro-3,6-dimethylpyrazine, and from the 1,4-di-N-oxide of 3,6-dimethylpyrazine, there resulted the 2,5-dichloro-3,6-dimethylpyrazine [4], i.e., in the case of pyrazine-N-oxides, substitution of chlorine proceeded only in the ortho-position to nitrogen oxidized. By analogy with the above-described examples, when mono-N-oxide ethyl ester of quinoxalyl-2-carboxylic acid was heated with $POCl_3$, formation of the chloro-derivative could only occur in the instance where nitrogen in the 4-position is oxidized, since in the case of 1-N-oxide, the ortho position to the nitrogen oxidized is occupied by the carbethoxy group. Upon treating the mono-N-oxide ethyl ester of quinoxalyl-2-carboxylic acid with $POCl_3$, there was isolated as the only reaction product a substance identical to the ethyl ester of 3-chloroquinoxalyl-2-carboxylic acid (V), earlier obtained from the ethyl ester of 3-hydroxyquinoxalyl-2-carboxylic acid. When reacted with Na_2CO_3 or NH_3, the authors obtained from it 3-chloroquinoxalyl-2-carboxylic acid and its amide [5]. It was thus proved that upon oxidizing quinoxalyl-2-carboxylic acid, or its ester, with H_2O_2, that the 4-N-oxides of these quinoxaline derivatives are formed. [See Scheme A on following page.]

The corresponding amide, hydrazide and hydroxamic acid were obtained from the 4-N-oxide ethyl ester of quinoxalyl-2-carboxylic acid (IV) when reacted with NH_3, NH_2NH_2 and NH_2OH.

1,4-Di-N-oxide of quinoxalyl-2-carboxylic acid (VII) could not be synthesized by direct oxidation of the initial acid. As was to be expected, the quinoxalyl-2-carboxylic acid reacted with H_2O_2, and the nitrogen in the ortho-position to the carboxyl group did not oxidize. The di-N-oxide of quinoxalyl-2-carboxylic acid (VII) was obtained in a roundabout way, namely by the oxidation of the 1,4-di-N-oxide-2-methylquinoxaline (VI) methyl group [6]. [See Scheme B on following page.]



A

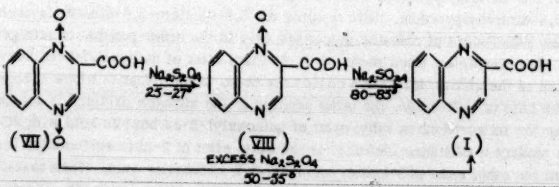
B

Oxidation of the di-N-oxide 2-methylquinoxaline methyl group was carried out in two stages: at first by action of SeO_2 on the aldehyde group, and then under mild conditions of H_2O_2 in glacial acetic acid at the carboxyl group. The oxidation carried out under more rigorous conditions led to rupture of oxygen or destruction of the quinoxaline ring.

Structure of 1,4-di-N-oxide quinoxalyl-2-carboxylic acid (VII), synthesized in such a manner, was proved by its reduction with $Na_2S_2O_4$ in alkaline medium, wherein it was possible to carry out gradual reduction (at 25-27°) to mono-N-oxide quinoxalyl-2-carboxylic acid, which then reduced to quinoxalyl-2-carboxylic acid (I) at 80-85°.

The mono-N-oxide resulting from reduction was not identical with the above-mentioned 4-N-oxide of quinoxalyl-2-carboxylic acid (III), thus making it possible to assign the only possible structure, 1-N-oxide quinoxalyl-2-carboxylic acid (VIII).

Reduction of 1,4-di-N-oxide quinoxalyl-2-carboxylic acid (VII) with large excess of $Na_2S_2O_4$ at 50-55° led immediately to the formation of quinoxalyl-2-carboxylic acid (I).



Thus, it was established that in 1,4-di-N-oxide quinoxalyl-2-carboxylic acid (VII), the first to be reduced was the N-oxide group which was in a meta-position to the carboxyl group; under more rigorous conditions, the N-oxide group in the position ortho to the carboxyl group, reduced first.

EXPERIMENTAL

Quinoxalyl-2-carboxylic Acid (I)

6.3 g of 2-(m-nitrostyrene)-quinoxaline in 200 ml of acetone was heated to boiling, cooled to 20°, and 5% aqueous solution of $KMnO_4$ added. The reaction mixture, after decolorization, was filtered off and the residue washed

with water. Acetone was distilled off from the combined filtrate. A mixture of acids was isolated with dilute hydrochloric acid from that remaining after distilling the aqueous acetone solution. The acid mixture was placed into 30 ml of 10% $NaHCO_3$ solution; thereupon, the sodium salt of quinoxalyl-2-carboxylic acid separated (10 ml of ethyl alcohol being added to complete precipitation of the sodium salt). Quinoxalyl-2-carboxylic acid was precipitated from aqueous solution of the sodium salt of quinoxalyl-2-carboxylic acid with dilute hydrochloric acid. The yield was 2.2 g (56.4%). M.p. 210-211° [2].

Ethyl ester of quinoxalyl-2-carboxylic acid (II) – colorless needles with m.p. 83-84°.

Quinoxalyl-2-aldehyde

18 g of SeO_2 was added slowly to a solution of 20 g 2-methylquinoxaline in 240 ml of toluene, with boiling. The reaction mixture was boiled for another 1.5 hours, filtered. Toluene was removed from the filtrate by steam, after which steam distillation was continued until the characteristic reaction of aldehyde with phenylhydrazine disappeared from the distillate. Quinoxalyl-2-aldehyde was salted out from the aqueous distillate with sodium chloride and the ether extracted. Yield of quinoxalyl-2-aldehyde after recrystallization from petroleum ether was 12.4 g (56.8%). M.p. 110° [2].

4.8 g (19.8%) of quinoxalyl-2-carboxylic acid was extracted from the selenium residue after repeated treatment with boiling water. M.p. 209-210° (decomposition).

Thiosemicarbazone of Quinoxalyl-2-aldehyde

A light-yellow, crystalline substance was obtained from 0.3 g of quinoxalyl-2-aldehyde in 5 ml of ethyl alcohol with 0.2 g of thiosemicarbazide in 5 ml of water, poorly soluble in organic solvents. M.p. 238-239° (decomposition).

4.265 mg sub.: 8.161 mg CO_2; 1.599 mg H_2O. 8.265 mg sub.: 3.61 ml 0.01 N I_2. 13.467 mg sub.: 5.77 ml 0.01 N I_2. Found %: C 52.18; H 4.2; S 14.00, 13.74. $C_{10}H_9N_5S$. Calculated %: C 51.97; H 3.92; S 13.86.

Quinoxalyl-2-carboxylic Acid from Quinoxalyl-2-aldehyde

$KMnO_4$ solution was added at room temperature to a solution of 0.2 g of quinoxalyl-2-aldehyde in acetone until decolorization ceased. The reaction mixture was filtered, and the quinoxalyl-2-carboxylic acid precipitated from the filtrate. Yield was 0.4 g (72.7%). M.p. 209-210°.

4-N-Oxide of Quinoxalyl-2-carboxylic Acid Ethyl Ester (IV)

23 ml of 30% H_2O_2, preheated for 3 hours at 40-45°, was added to a mixture of 25 ml glacial CH_3COOH and 19.2 ml of acetic anhydride, and 4.75 g of the ethyl ester of quinoxalyl-2-carboxylic acid added. Oxidation was carried out for 16 hours at 50°, the reaction solution cooled, the acetic acid neutralized with $NaHCO_3$, and the resulting 4-N-oxide of the ethyl ester of quinoxalyl-2-carboxylic acid filtered off; yellow needles, poorly soluble in water, relatively readily-soluble in methyl and ethyl alcohols. It precipitated iodine from KI solutions. The yield was 4.1 g (80.1%). M.p. 156-157° (from CH_3OH).

5.225 mg sub.: 4.78 ml 0.01 N H_2SO_4. 3.270 mg sub.: 2.95 ml 0.01 N H_2SO_4. Found %: N 12.81, 12.64. $C_{11}H_{10}O_3N_2$. Calculated %: N 12.84.

4-N-Oxide of Quinoxalyl-2-carboxylic Acid (III)

a) 1 g of quinoxalyl-2-carboxylic acid was added to a mixture of 15 ml of glacial CH_3COOH, 4.7 ml of acetic anhydride and 5.6 ml of H_2O_2 (30%), preheated for 3 hours at 45-50°, and heating was continued at 50° for 16 hours. The reaction solution was then evaporated in vacuo (bath temperature 40-45°) to $\frac{1}{3}$ volume, cooled, and the 4-N-oxide of quinoxalyl-2-carboxylic acid filtered off, which was purified either by precipitation from bicarbonate solution or by crystallization from alcohol. The yield was 0.8 g. M.p. 180-182°. A sample mixed with 4-N-oxide of quinoxalyl-2-carboxylic acid, obtained by saponification of the corresponding ester, melted without depression.

6.333 mg sub.: 6.03 ml 0.01 N H_2SO_4. 6.228 mg sub.: 5.98 ml 0.01 N H_2SO_4. Found %: N 13.32, 13.45. $C_9H_6O_3N_2 \cdot H_2O$. Calculated %: N 13.46.

b) 2 g of the ethyl ester of quinoxalyl-2-carboxylic acid 4-N-oxide was stirred for 20 minutes with 20 ml of 7.5% NaOH solution. 80 ml of water was added to the reaction mixture, the solution decolorized with activated carbon, and filtered. The filtrate was acidified with hydrochloric acid to acid reaction for Congo red; 4-N-oxide of quinoxalyl-2-carboxylic acid separated – a light yellow crystalline compound, poorly soluble in water, soluble with heat in ethyl and methyl alcohols. Yield was 1.76 g. M.p. 180-182° (from ethyl alcohol).

4-N-Oxide Amide of Quinoxalyl-2-carboxylic Acid

0.3 g of the 4-N-oxide ethyl ester of quinoxalyl-2-carboxylic acid was left at room temperature for 12 hours with 3 ml of an alcoholic solution of NH_3. The 4-N-oxide amide of quinoxalyl-2-carboxylic acid (0.85 g) which separated out was filtered off and crystallized from C_2H_5OH. Light-yellow crystalline substance, m.p. 230-230.5°.

3.110 mg sub.: 4.87 ml 0.01 N H_2SO_4. 4.200 mg sub.: 6.64 ml 0.01 N H_2SO_4. Found %: N 21.92, 22.13. $C_9H_7O_2N_3$. Calculated %: N 22.22.

4-N-Oxide Hydrazide of Quinoxalyl-2-carboxylic Acid

0.34 ml of 85% H_2N-NH_2 was added to 1 g of the N-oxide ethyl ester of quinoxalyl-2-carboxylic acid in 1 ml of anhydrous C_2H_5OH. The mixture was left for 12 hours at room temperature. The N-oxide hydrazide of quinoxalyl-2-carboxylic acid (0.9 g) which separated in the form of slightly yellow crystals, was filtered off and crystallized from 50% C_2H_5OH. M.p. 216-217°.

3.532 mg sub.: 6.856 mg CO_2; 1.281 mg H_2O. Found %: C 52.97; H 4.06. $C_9H_8O_2N_4$. Calculated %: C 52.91; H 3.95.

4-N-Oxide of Quinoxalyl-2-hydroxamic Acid

1.97 g of KOH in 29 ml of methanol was added with stirring to 1.64 g of $NH_2OH \cdot HCl$ in 9 ml of CH_3OH. 2 g of the 4-N-oxide of the ethyl ester of quinoxalyl-2-carboxylic acid was introduced into the reaction mixture cooled to 40°, and left at room temperature for 20 hours. The resulting potassium salt of 4-N-oxide quinoxalyl-2-hydroxamic acid was filtered off and the free acid (1.7 g) obtained by addition of 6 ml of CH_3COOH (1.25 normal). Slightly yellow crystals, m.p. 185-186° (from water).

3.879 mg sub.: 7.469 mg CO_2; 1.164 mg H_2O. 3.657 mg sub.: 7.060 mg CO_2; 1.120 mg H_2O. 2.500 mg sub.: 3.620 ml 0.01 N H_2SO_4. Found %: C 52.55, 52.68; H 3.36, 3.42; N 20.27. $C_9H_7O_3N_3$. Calculated %: C 52.66; H 3.44; N 20.49.

Reduction of the 4-N-Oxide of Quinoxalyl-2-carboxylic Acid

0.5 g of $Na_2S_2O_4$ was gradually added, with stirring, to 0.3 g of 4-N-oxide quinoxalyl-2-carboxylic acid solution in 3.5 ml of 15% NaOH and 22 ml of water. After standing for one hour at rooom temperature, the reaction solution was acidified to a weak acid reaction for Congo red. Quinoxalyl-2-carboxylic acid which separated was filtered off and precipitated from bicarbonate solution. Yield was 0.23 g (83.9%). M.p. 210-211°. A sample mixed with quinoxalyl-2-carboxylic acid obtained by oxidation of 2-(m-nitrostyryl)-quinoxaline melted without depression.

Interaction of the 4-N-Oxide Ethyl Ester of Quinoxalyl-2-carboxylic Acid with $POCl_3$ (Ethyl Ester of 3-Chloroquinoxalyl-2-carboxylic Acid, V)

A solution of 1 g of the ethyl ester of 4-N-oxide quinoxalyl-2-carboxylic acid in 10 ml of $POCl_3$ was boiled for 1.5 hours, and the $POCl_3$ then distilled off to half-volume, the residue being poured into water with ice and alkalized with $NaHCO_3$. The ethyl ester of 3-chloroquinoxalyl-2-carboxylic acid was extracted with ether. The ether extract was washed with water, dried with Na_2SO_4, and the ether distilled off. The residue was crystallized from 70% methyl alcohol. Ethyl ester of 3-chloroquinoxalyl-2-carboxylic acid — almost colorless crystals with m.p. 41.5-42° [5].

3-Chloroquinoxalyl-2-carboxylic Acid

A solution of 0.25 g of the ethyl ester of 3-chloroquinoxalyl-2-carboxylic acid and 0.07 g of Na_2CO_3 in 13 ml of 70% methyl alcohol was heated at 60-70° for 1.5 hours. The methyl alcohol was distilled off in vacuo at 25-30°. The residue was dissolved in water, acidified, and the resulting 3-chloroquinoxalyl-2-carboxylic acid crystallized from water. 0.15 g of acid resulted with m.p. 146-147° (decomposition) [5].

3-Chloroquinoxalyl-2-carboxylic Acid Amide

Obtained from 0.1 g of the ethyl ester of 3-chloroquinoxalyl-2-carboxylic acid upon passing a dry stream of NH_3 into an alcoholic solution of the ester at 0°. The resulting 3-chloroquinoxalyl-2-carboxylic acid amide melted at 214-215° [5].

1,4-di-N-Oxide of Quinoxalyl-2-aldehyde

3.5 g of SeO_2 was gradually added with stirring to a boiling solution of 1,4-di-N-oxide-2-methylquinoxaline (3 g) in 100 ml of benzene. The reaction mixture was boiled for another 2 hours, filtered, and benzene distilled off from the filtrate to $\frac{1}{3}$ of the initial volume, and the resulting 1,4-N-oxide of quinoxalyl-2-aldehyde (2.02 g)

filtered off. An orange-yellow crystalline compound, poorly soluble in standard organic solvents and in water, m.p. 189-190° with decomposition (from benzene) gave characteristic reactions for aldehyde (hydrazones, semicarbazones) and precipitated I_2 from acid solutions of KI (reaction characteristic for N-oxides).

4.810 mg sub.: 0.637 ml N_2 (24°, 726 mm). 3.233 mg sub.: 6.700 mg CO_2; 0.918 mg H_2O. 3.340 mg sub.: 6.936 mg CO_2; 0.931 mg H_2O. Found %: N 14.54; C 56.56, 56.67; H 3.17, 3.11. $C_9H_6O_3N_2$. Calculated %: N 14.73; C 56.82; H 3.17

1,4-di-N-Oxide of Quinoxalyl-2-carboxylic Acid (VII)

1 g of 1,4-di-N-oxide quinoxalyl-2-aldehyde was added to a mixture of 16 ml of glacial CH_3COOH, 5 ml of H_2O_2 (30%) and 2 ml of acetic anhydride, preheated to 40-50° (for 3 hours). The reaction solution was heated at 50° for 1 hour, and was then cooled and 1,4-di-N-oxide quinoxalyl-2-carboxylic acid was filtered off. Bright-yellow crystalline compound, poorly soluble in standard organic solvents. Precipitated iodine from acid KI solution. M.p. 208-209° (from acetic acid). Yield was 0.76 g (68.2%).

6.490 mg sub.: 6.260 ml 0.01 N H_2SO_4. 3.925 mg sub.: 7.520 mg CO_2; 1.12 mg H_2O. 4.135 mg sub.: 7.927 mg CO_2; 1.116 mg H_2O. Found %: N 13.5; C 52.29, 52.32; H 3.18, 3.02. $C_9H_6O_4N_2$. Calculated %: N 13.59; C 52.41; H 2.94.

Reduction of 1,4-di-N-Oxide Quinoxalyl-2-carboxylic Acid to 1-N-Oxide Quinoxalyl-2-carboxylic Acid (VIII)

0.15 g of $Na_2S_2O_4$ was added, with stirring, to a solution of 0.2 g of 1,4-di-N-oxide quinoxalyl-2-carboxylic acid in 10 ml of 5% NaOH solution at 20-25°. After standing for 10 minutes, the solution was filtered. The filtrate was acidified to an acid reaction with Congo red, and the resulting acid (0.12 g) was filtered off and purified by acid reprecipitation from bicarbonate solution. 1-N-oxide quinoxalyl-2-carboxylic acid – a colorless crystalline compound with m.p. 180-181° – precipitated iodine from acid KI solution. A sample mixed with 4-N-oxide quinoxalyl-2-carboxylic acid melted at 160-163°.

5.068 mg sub.: 5.35 ml 0.01 N H_2SO_4. Found %: N 14.77. $C_9H_6O_2N_2$. Calculated %: N 14.74.

Reduction of 1-N-Oxide Quinoxalyl-2-carboxylic Acid to Quinoxalyl-2-carboxylic Acid (I)

0.25 g of $Na_2S_2O_4$ was added, with stirring to a solution of 0.1 g of 1-N-oxide quinoxalyl-2-carboxylic acid in 15 ml of 3% NaOH solution. The reaction solution was stirred for 1 hour at 80-85°, and was then treated with activated carbon and filtered. The filtrate was acidified with HCl (1:3) to an acid Congo red reaction. The resulting acid (0.07 g) was distilled off, melting point 208-209°; the N-oxide group was not found. A sample of the resulting mixture with quinoxalyl-2-carboxylic acid, prepared by oxidation of quinoxalyl-2-aldehyde, melted without depression.

SUMMARY

1. It has been established that the 4-N-oxide of the acid is formed upon oxidation of quinoxalyl-2-carboxylic acid with H_2O_2 in glacial CH_3COOH. The structure of the resulting compound has been proved by its conversion to the intial quinoxalyl-2-carboxylic acid, through reduction of the N-oxide group with $Na_2S_2O_4$ in alkaline medium, as well as by formation of its ethyl ester by interaction with $POCl_3$, to form 3-chloroquinoxalyl-2-carboxylic acid ethyl ester.

2. 1,4-di-N-oxide quinoxalyl-2-carboxylic acid has been obtained by gradual oxidation of the 1,4-di-N-oxide-2-methylquinoxaline methyl group, first to the aldehyde (SeO_2 in boiling benzene), and then to the carboxyl group (H_2O_2 in glacial CH_3COOH).

3. It has been determined that upon reducing 1,4-di-N-oxide quinoxalyl-2-carboxylic acid with $Na_2S_2O_4$ in alkaline solution, the N-oxide group meta to the carboxyl is first of all reduced, and then the second N-oxide group which is ortho to the carboxyl.

LITERATURE CITED

[1] G. T. Newbold, F. S. Spring, J. Chem. Soc., 1948, 519.
[2] W. Boersche, W. Doeller, Ann., 537, 39 (1938).
[3] O. Yu. Magidson and M. V. Rubtsov, J. Gen. Chem., 7, 1896 (1937); I. Meisenheimer, Ber., 59, 1848 (1926); B. Bobransku, L. Kochanska, A. Kowalewska, Ber., 71, 2385 (1938).
[4] G. T. Newbold, F. S. Spring, J. Chem. Soc., 1947, 1183.
[5] A. H. Gowenlock, G. T. Newbold, F. S. Spring, J. Chem. Soc., 1945, 622.
[6] H. McIlwain, J. Chem. Soc., 1943, 322.

Received April 24, 1954

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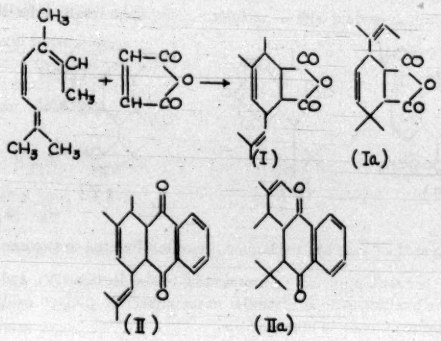
THE STRUCTURES OF MALEIC ANHYDRIDE AND α-NAPHTHOQUINONE ADDITION PRODUCTS TO ALLOOCYMENE

B. A. Arbuzov and A. R. Vilchinskaya

Alloocymene, a compound with conjugated double bonds, adds readily maleic anhydride, α-naphthoquinone and other dienophiles.

Structures (I) and (Ia) can be attributed to the maleic anhydride addition product, and to α-naphthoquinone – (II) and (IIa).



In the previous works [1], no final choice was made by one of us as between (I) and (Ia) and between (II) and (IIa).

During dehydrogenation of the α-naphthoquinone addition product with air in the presence of potassium hydroxide, there resulted a product with m.p. 119-120°, which, according to analysis, did not correspond to the anthraquinone derivative, but to the dihydroanthraquinone derivative, which pointed to a greater probability for structure (IIa). There could have been expected to result, upon dehydrogenation of the product of structure (II) followed by oxidation with nitric acid, anthraquinone-1,2,4-tricarboxylic acid, which failed to separate, however, in the earlier works.

The data obtained permitted one of us to consider formula (IIa) as more probable for the addition of alloocymene to α-naphthoquinone. On the other hand, addition of dienophiles to a conjugated alloocymene system, with formation of products (I) and (II) is more understandable, since carbons 4 and 7 are less substituted than 2 and 5.

The obscurity of addition of maleic anhydride and α-naphthoquinone to alloocymene prompted the authors to return again to the problem.

Choice between structure (I) and (Ia), and correspondingly between (II) and (IIa), could be made on the basis of ozonization products of the addition products. With structures (I) and (II) for the addition products, acetone should result on decomposition of the ozonides, and with structures (Ia) and (IIa) – acetaldehyde.

Ozonization of the addition product with maleic anhydride, and decomposition of the ozonide with water gave acetone identified by its dibenzalacetone (m.p. 111-112°), the semicarbazone (m.p. 126-128°) and the 2,4-dinitrophenylhydrazone (m.p. 124-125°). By a quantitative determination of acetone obtained by decomposition of the ozonized addition product in soda solution, the authors obtained 62.3% acetone. Decomposition of other ozonides gave resinous substances, from which it was not possible to separate individual compounds.

Acetone was also found on ozonization of the addition product of α-naphthoquinone. Acetaldehyde was not found in any of these experiments.

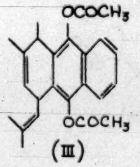
The data obtained made it possible to attribute formula (I) to the addition product with maleic anhydride, and formula (II) to the addition product with α-naphthoquinone.

The authors repeated oxidation experiments, using dilute nitric acid, on the dehydrogenated addition product of α-naphthoquinone, to obtain anthraquinonetricarboxylic acid. The oxidation product, after purification by subliming, was in the form of fine, needle crystals, yellow in color, with an indefinite melting point of 270-280°. From reaction of its silver salt with methyl iodide, the methyl ester resulted (m.p. 191.5-193°), which, according to the literature data, corresponded to the trimethyl ester of anthraquinonetricarboxylic-1,2,4 acid [2].

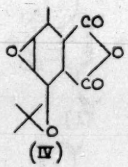
The authors attempted other methods for oxidation of the α-naphthoquinone addition product: heating with sulfur at 200°, with selenium, with palladinized carbon, and by heating in nitrobenzene. Resinification occurred in all cases.

In the course of study of alloocymene addition products with α-naphthoquinone and maleic anhydride, the authors obtained some derivatives of these compounds which have not been described in the literature.

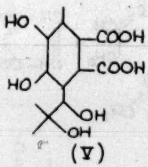
By acetylation of the addition product with α-naphthoquinone, there resulted the diacetate (III), m.p. 143-144°.



(III)



(IV)



(V)

On reacting the addition product with hydroxylamine, there resulted the monoxime (m.p. 183°).

Two products resulted: one with m.p. 145°, corresponding to the dioxide (IV), and one with m.p. 190-191°, corresponding, according to the analysis, to an acid similar to the anhydride (IV), on oxidizing the maleic anhydride addition product with acetyl hydroperoxide in ether solution.

Upon dehydrating the 145° melting oxide with acidified water, two substances resulted, m.p. 172° (decomposition) and m.p. 277° (decomposition). The latter compound corresponded to the dilactone of the tetrahydroxy acid (V), according to analysis.

Upon oxidizing the addition product of maleic anhydride with potassium permanganate, according to the method of E. E. Wagner, two products were isolated: one with m.p. 145-146° (foaming), which corresponded closely to the tetrahydroxy acid (V), according to analysis, and the other with m.p. 223-224° (decomposition), corresponding to the dihydroxy acid, according to analysis. Saturation in the compound melting at 223-224° (oxidation with perphthalic acid) made possible the formation of a lactone at the expense of interaction of the double bond with the carboxyl group.

The structures of the enumerated products were not determined.

EXPERIMENTAL

Ozonization of the alloocymene addition product with maleic anhydride. a) 10 g of the addition product was dissolved in 50 ml of chloroform. A stream of ozone was passed through the solution for 5 hours. After freeing from solvent, the ozonide, as a slightly-yellow, thick mass, was heated on a water bath with 50 ml of water under reflux for 6 hours. The greater portion of ozonide dissolved. From the aqueous distillate, after reacting with benzaldehyde, dibenzalacetone (m.p. 111-112°) resulted. Acetone semicarbazone (m.p. 126-128°) was obtained with semicarbazide.

There resulted upon oxidation of the residue by hydrogen peroxide, a resinous product after distilling off the water, from which it was not possible to isolate any crystalline compounds.

b) The addition product was ozonized in carbon tetrachloride. The ozonide was obtained as a white powder, decomposing at 75-90°. After decomposing the ozonide with boiling water, acetone 2,4-dinitrophenylhydrazone (m.p. 124-125°, from alcohol) was obtained from the aqueous distillate plus 2,4-dinitrophenylhydrazine.

Ozonization of the sodium salt of the addition product. The addition product (2 g) was dissolved in soda solution (2.4 g $Na_2CO_3 \cdot 10H_2O$ and 20 g water) by shaking for 10 days. Acetone was determined according to the Messinger [3] method after ozonizing the aqueous solution and decomposing the ozonide. Acetone found was 62.3%.

Oxidation of the addition product with a dilute solution of potassium permanganate. The addition product (13.2 g) was dissolved in alkali (4.5 g of sodium hydroxide) and was then oxidized with a 0.5-1% solution of potassium permanganate (11.7 g) in water (1,370 ml) with ice-cooling. Two products were isolated with m.p. 145-146° (foaming) and m.p. 223-224° (decomposition), after saturating the solution with carbon dioxide, evaporating in a stream of carbon dioxide, and acidifying with phosphoric acid.

Analysis of the substance with m.p. 145-146°

Found %: C 52.55; H 7.57. $C_{14}H_{24}O_3$. Calculated %: C 52.46; H 7.55

Analysis of the substance with m.p. 223-224°

Found %: C 58.65; H 7.88. $C_{14}H_{22}O_6$. Calculated %: C 58.70; H 7.75.

Perphthalic acid titration did not show any unsaturation in the product.

Oxidation with acetyl hydroperoxide of the addition product with maleic anhydride. 10 g of the addition product was gradually added to a solution of 8 g of acetyl hydroperoxide in 112 ml of ether. The temperature rose from 17° to 35°. After 24 hours, there separated out to the bottom of the flask white crystals in the form of needles arranged in small rosettes. After washing with ether, the m.p. was 135-139°. After recrystallization from ether the m.p. was 145°.

Found %: C 63.25; H 6.83. $C_{14}H_{18}O_5$. Calculated %: C 63.12; H 6.81.

After removal of ether from the filtrate, crystals of m.p. 165-171° resulted in vacuo. After recrystallization from alcohol, m.p. was 190-191°.

Found %: C 59.33, 59.26; H 7.03, 7.12. $C_{14}H_{20}O_6$. Calculated %: C 59.12; H 7.09.

Hydration of the oxide. 2 g of the oxide with m.p. 145° was shaken for 7 days with 25 ml of water and 5 ml of concentrated sulfuric acid. The resulting precipitate melted within the range of 212-225°. After repeated fractional recrystallizations from water, alcohol and ether, two products of m.p. 172° (decomposition) were isolated, apparently representing the monolactone with dilactone impurities.

Found %: C 56.03; H 7.07. $C_{14}H_{22}O_7$. Calculated %: C 55.59; H 7.33.

The other product has a m.p. of 277° (decomposition), and from its composition corresponded to the tetrahydroxy acid dilactone.

Found %: C 59.13; H 7.09. $C_{14}H_{20}O_6$. Calculated %: C 59.12; H 7.09.

Ozonization of the alloocymene addition product with α-naphthoquinone. A stream of ozone gas was passed through 10 g of the addition product in 50 ml of chloroform for 9 hours. The ozonide precipitated as a glassy mass. After removal of the chloroform, the ozonide was decomposed with water on a water bath for 3 hours. Complete dissolution of the ozonide did not occur. After distilling off the water, acetone was found in the residue by means of the iodoform reaction and synthesis of dibenzalacetone (m.p. 112°). Quantitative determination of acetone gave, according to Messinger [3] 26.5%.

Ozonization of the dehydrogenated addition product with α-naphthoquinone. 3.5 g of the product, dehydrogenated by passing air through in the presence of potassium hydroxide, was dissolved in 35 ml of carbon tetrachloride and ozonized for 8 hours. The solid, dark brown-colored ozonide was decomposed by the usual method with water. Dibenzalacetone with m.p. 112° was obtained from the aqueous distillate with benzaldehyde.

Oxidation of the dehydrogenated addition product with nitric acid. The dehydrogenated product, with m.p. 119-120° (1.4 g) was sealed with 20 ml of nitric acid (d 1.1) in a test tube. The test tube was heated carefully to 195°. After removal of the gases, the heating temperature was brought up to 230°. Heating was continued for 5 hours. The resulting precipitate, yellow in color, was washed with water and dried. The product shrank at 250°, and at 285° it foamed and darkened. Upon sublimation, thin yellow needles resulted. It melted in the range 270-280°.

A silver salt was prepared from 0.5 g of the product. Excess methyl iodide (20 g) was added to the salt. A vigorous reaction took place. The entire mixture was heated for 2.5 hours on a water bath with a reflux condenser.

After filtering and evaporating off the methyl iodide, the residue (0.35 g) melted at 175-185°. After two recrystallizations from acetoacetic ester, the m.p. was 191.5-193°. 1,2,4-Anthraquinonetricarboxylic acid trimethyl ester has a m.p. of 193°.

Acetylation of the alloocymene addition product with α-naphthoquinone. The addition product (5.8 g) and 25 ml of freshly-distilled acetic anhydride containing one drop of concentrated sulfuric acid was heated for 2 hours with a reflux condenser. The excess acetic anhydride was removed in vacuo. The crystalline precipitate, after two recrystallizations from benzene, had a m.p. of 140-141° (3 g). After two additional recrystallizations from alcohol, the m.p. was 143-144°.

Found %: C 76.09; H 6.76. $C_{24}H_{26}O_4$. Calculated %: C 76.19; H 6.87.

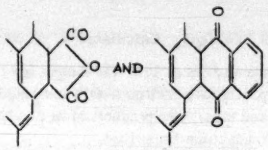
Synthesis of the oxime of the addition product between α-naphthoquinone and alloocymene. The addition product (3 g), 2 g of hydroxylamine hydrochloride, 3 g of sodium acetate, and 20 ml of methyl alcohol were heated on a water bath for 2 hours. After filtering off from the sodium chloride, and diluting the filtrate, a resin precipitated. When dissolved in hot alcohol, crystals precipitated. After several recrystallizations from alcohol and gasoline, crystals of m.p. 175° resulted. At 183° foaming occurred. The product crystallized in the form of needles and cubes. The melting point of both forms of crystals was the same.

Found %: C 77.75; H 7.32. $C_{20}H_{23}O_2N$. Calculated %: C 77.67; H 7.44.

Thus, analysis corresponded to the monooxime.

SUMMARY

1. Ozonization of alloocymene addition products with maleic anhydride and with α-naphthoquinone, with subsequent rupture of the ozonides, leads to formation of acetone, indicating the following structure for the addition products:



2. A number of alloocymene addition products with maleic anhydride and with α-naphthoquinone have been described.

LITERATURE CITED

[1] B. A. Arbuzov, J. Gen. Chem., 3, 28 (1933); 6, 206 (1936).

[2] A. Dansi, Chem. Zentr., 937, II, 1368; Cook, Chem. Zentr., 1932, I, 64.

[3] See Thorpe and Whitely, "Practical Manual for Organic Analysis", page 196.

Received May 29, 1954

Kazan State University and State Institute of Medicine

INVESTIGATION OF THE ESTER OIL FROM ZAILYSK WORMWOOD

ARTEMISIA TRANSILIENSIS P. POL.

M. I. Goryaev and M. G. Pugachev

Upon comparing the composition of eucalyptus ester oils, which have wide application abroad in medicine and industry, with ester oils from certain varieties of wormwoods which grow in the USSR, the authors have found considerable similarities among them. The principal constituent of these oils is found to be either eucalyptol or cineol. Both eucalyptus oil and its principal constituent, cineol, were recognized long ago, and are used in medicine as antiseptics and anesthetics. Their usage is limited in the Soviet Union, however, and is represented only by one form of wormwood oil which contains 70-80% cineol.

Investigations of the authors have demonstrated that, besides Artemisia cina, the cineol oils are contained in a variety of wormwoods, and in particular, the ester oil of Zailysk wormwood, which, as studied for the first time by the authors, contains more than 55% cineol. This plant has been tested in large scale culture, and the ester oils offer definite interest to industry.

EXPERIMENTAL

The ester oil of Zailysk wormwood was prepared by the authors for investigation, from the wild species which was collected in the area of the city of Alma-Ata during the flowering stage. Upon steam distilling 685.8 kilograms of the above-ground portion of wormwood having a moisture content of 24.8%, there resulted 2 kilograms of ester oil, or 0.4%. The oil was lemon-yellow in color, with a bitter taste, and the aroma of cineol-camphor. After drying with Na_2SO_4 and filtering, the oil had the following constants:

d_{20}^{20} 0.9306, n_D^{20} 1.4670, $[\alpha]_D^{20}$ −12.3°, acid number 2.56, ester number 26, ester number after acetylation 47.78, σ 34.9 dynes/cm.

The oil was soluble in 90% alcohol in all proportions, in 80% to the extent of a 1:0.8 ratio. The presence of aldehydes, ketones, phenols, azulene-forming sesquiterpenes and cineol were demonstrated by qualitative tests. Sulfur and nitrogen reactions were negative.

Qualitative identification of cineol was carried out by synthesis of a crystalline compound with 50% aqueous resorcinol solution. The cineol-resorcinol, after two recrystallizations from 70% alcohol, had a m.p. of 82-83°. Its oxidation to cineolic acid [1] was carried out for identification of cineol. Cineol was isolated from the cineol-resorcinol complex by decomposition with 10% Na_2CO_3 solution, which, after distillation, possessed the following constants:

b.p. 176-177°, d_4^{20} 0.9268, n_D^{20} 1.4583.

3 g of cineol, 15 g of potassium permanganate and 3,225 ml of water were taken for the oxidation. The mixture was heated on a water bath to the point of permanganate decolorization. 0.21 g of cineolic acid with m.p. 196-197° (decomposition resulted from the oxidation).

Quantitative determination of cineol. 10 ml of the ester oil was treated with 50% aqueous resorcinol solution. The precipitated crystals of cineol-resorcinol were filtered off, and then pressed between sheets of filter paper for complete removal of moisture, and weighed. The cineol content was found to be 57% from the cineol-resorcinol complex $(C_{10}H_{18}O)_2 \cdot C_6H_6O_2$. The cineol-resorcinol was decomposed with 10% NaOH solution, and the liberated cineol was distilled with steam. 5.53 ml of cineol was obtained, constituting 55.3% of the oil taken. The cineol content was once more verified by a volumetric procedure, measuring the loss in volume of the investigated oil in a graduated Cassius flask upon transition of cineol into the aqueous resorcinol solution. The oil was diluted with 50% turpentine [2] in order to prevent precipitation of cineol-resorcinol crystals from the concentrated solution. 53% cineol was found by this method. The authors are inclined to believe that the true cineol content lies within the range of that found from the data on weight determination, and the amount found by steam distillation of the decomposed complex after weighing, i.e., between 55.3-57%, since the first method gave somewhat elevated, and the second, somewhat depressed data.

The averaged determinations of carbonyl compounds in the oil, as carried out by the bisulfate method [3], constituted 20,6 %.

Total phenols was determined by the volumetric method as well – by dissolution in 5% NaOH in a Cassius flask; 1,5% phenols was found in the oil after having removed beforehand the acid (by treating with 10% soda solution).

For further investigation, the oil was fractionated (at 700 mm) into 6 fractions with boiling point between 150 and 180°. The oil residue which did not fractionate up to 180° amounted to another 38,45%, which was fractionated in vacuo at 27mm; thereupon, 11 more fractions resulted, with b.p. 77 to 142°. For all the fractions there were determined specific weight, refraction, angle of rotation, acid number, ester number after acetylation. Fractionation indicated that the oil does not have components boiling below 150°. The principal portion of oil (54,5%) distilled at 170-180°. 33,38 g (8,62%) in the form of a crystalline, resinified mass, was in the residue from vacuum distillation. The oil possessed a green color in the last three fractions. The first fractions had a characteristic cineol odor, fading in the 5th fraction. Beginning with this latter fraction, and higher, the cineol test with resorcinol was negative. Judging from the acid number, the acids were concentrated in the second fraction. As determined by the authors, in this case free formic and isobutyric acids; in the last fractions (between 85-142°), the acid number increased at the expense of phenol accumulation, which was evident from the coloration of these fractions with ferric chloride, and by the absence of acid extracts with 10% soda solution. It can be seen from a comparison of the ester numbers before and after acetylation, that the presence of two alcohols is possible; one of them in the free state and in the form of an ester concentrated in the 150-160° fraction; the second in the fraction 95-142° (27 mm).

Formic acid assumed to be present in the 1st fraction was demonstrated and determined quantitatively [4].

For this purpose, 4,02 g of oil was neutralized with 0,1 N KOH, the aqueous layer separated, and 4,5 g of mercuric chloride in water solution added to it. The flask was covered with a stopper containing a long tube as air condenser, and the sample heated on a water bath for 8 hours. The solution rapidly became turbid, evolved CO_2 bubbles, and formed a voluminous calomel precipitate. After 5 hours, the solution became completely transparent. The weight of calomel precipitate was 0,348 g. Calculating from the $HCOOK + 2HgCl_2 \longrightarrow$ $\longrightarrow 2HgCl + CO_2 + HCl + KCl$ equation, the quantity of formic acid was found to be 0,84% in relation to the fraction, or 0,01% of the original oil.

For the second fraction, the authors made an assumption that isobutyric acid was present, which was confirmed by synthesis of the anilide [5].

For this purpose, 6,24 g of the fraction boiling at 155-160° was neutralized with NaOH. The water layer, containing the sodium salt of the acid was evaporated in a porcelain dish. The dry sodium salt weighed 0,013 g. The Na salt of the acid was mixed with 1 ml of freshly-distilled aniline and 0,3 ml of concentrated HCl in a test tube. White crystals of the anilide precipitated after heating for 1 hour. The anilide recrystallized from alcohol melted at 103°, which corresponded to isobutyric acid. Calculating from the acid number for the fraction 0,0086% isobutyric acid was found in the oil.

From its odor, the first fraction resembled pinene after freeing from acids and cineol. For proof of α-pinene, the sample was oxidized with 1% $KMnO_4$ in the cold. The semicarbazone from the resulting keto acid melted at 202-203°, i.e., corresponding to pinonic acid, proving the presence of α-pinene. An attempt to determine β-pinene in the 2nd fraction by synthesis of pinonic acid did not lead to the expected results. Upon testing for phellandrene in the fraction from 170 to 189°, phellandrene nitrosite was not obtained.

200 g of the initial oil was mixed with 600 ml of saturated $NaHSO_3$ solution, to study carbonyl compounds. After vigorous shaking for 1-2 hours, a white voluminous precipitate of the double bisulfite compound separated. The precipitate was purified with alcohol and decomposed with 20% soda solution, the oil which separated being distilled off with steam. 43,3 g of carbonyl compounds was obtained, which were fractionated in vacuo at 7 mm into 8 fractions with b.p. from 48 to 90° for further analysis.

The 3rd fraction (b.p. 55-60° at 7 mm, d_{20}^{20} 0,9179, n_D^{20} 1,4527, $[\alpha]_D$ + 28,7°) and the 4th fraction (b.p. 60-65° at 7 mm, d_{20}^{20} 0,9170, n_D^{20} 1,4530, $[\alpha]_D$ + 28,3°) gave a semicarbazone with m.p. 158-160°, the tribromide (according to the Wallach [6] method), melting at 120-121°, and the 2,4-dinitrophenylhydrazone [7], melting at 104-106° (from methyl alcohol), $[\alpha]_D$ + 29°10' [8]. It could be assumed from the angle of rotation that the mixture of α- and β-thujones was separated by the authors.

The 7th fraction (d_{20}^{20} 0,9642, n_D^{20} 1,5194, $[\alpha]_D$ + 0,2°) and the 8th fraction (d_{20}^{20} 0,9790, n_D^{20} 1,5279, $[\alpha]_D$ 0°) resembled cumic aldehyde in odor.

M (for the combined fraction, as determined by the method of Rast) 148.64. $C_{10}H_{12}O$. Calculated: M 148.20. MR_D 46.89, calculated 46.83. The semicarbazone, m.p. 208-210°; 2,4-dinitrophenylhydrazone – carmine-red needles with m.p. 240-243°; phenylhydrazone, thin light-yellow needles, m.p. 128-129°.

The cumic alcohol was oxidized with silver oxide [8]. For this purpose, 1.5 g of the substance in 60 ml of alcohol not containing any aldehyde impurities, and 3.5 g of silver nitrate in 10 ml of water, were taken. 75 ml was treated with 0.5 N-sodium hydroxide for 0.5 hour. The filtrate was saturated with carbon dioxide and then concentrated on a water bath to $\frac{1}{3}$ of its original volume, acidified with hydrochloric acid, and the resulting acid extracted with ether. 1.4456 g of cumic acid resulted, and after two recrystallizations, melted at 110-112° (from alcohol). Cumic alcohol oxidizes directly with oxygen of the air. The acid was isolated as a thin layer from alcohol, three days after pouring into beakers, and the acid isolated melted, after recrystallization, at 112-113°, which coincided closely with that of the literature data for cumic acid [9].

Analysis of the silver salt gave the following results:

Found %: Ag 39.77. Calculated %: Ag 39.77.

Analysis of cumic aldehyde semicarbazone:

7.02 mg sub.: 16.60 mg CO_2; 4.72 mg H_2O. 7.92 mg sub.: 18.68 mg CO_2; 5.35 mg H_2O. 3.23 mg sub.: 0.617 ml N_2 (23°, 689 mm). 3.42 mg sub.: 0.666 ml N_2 (22°, 692 mm). Found %: C 64.53, 64.35; H 7.52, 7.56; N 20.54, 20.52. $C_{11}H_{16}N_3O$. Calculated %: C 64.54; H 7.32; N 20.37.

The absorption spectrum for the given aldehyde gave 3 maxima: 323, 275 and 255 mμ. The authors did not have access to literature data on cumic alcohol absorption spectra; for benzaldehyde, which approximates cumic alcohol in structure, the following spectra are quoted, which also have 3 maxima: 333, 280 and 246 mμ. Data quoted by the authors confirm the presence of cumic aldehyde.

Identification of phenols. The fraction with b.p. from 85 to 142° (7 ml) was colored by alcoholic and aqueous $FeCl_3$ solutions. For isolation of the phenols, each fraction was separately treated with 5% KOH solution, the alkaline extracts were combined, washed free of traces of oil with ether, and saturated with CO_2. The phenols which separated out in the amount of 4.1 g possessed a burning taste and a characteristic cresol odor: d_{20}^{20} 1.0255, n_D^{20} 1.5245. Brown-violet coloration was displayed with alcoholic and aqueous $FeCl_3$. The Denige formaldehyde reaction [10] gave a violet coloration and formation of a turbidity, the color disappearing upon addition of alcohol. The acetaldehyde reaction of Denige produced a yellow-orange color, converting to yellow-brown. Both of these qualitative reactions are characteristic for m-cresol.

The fractions from 170-180° contained about 5% of free and bound alcohols in the form of esters. On the basis of phthalic acid ester synthesis, it was established that the alcohols are secondary. In order to identify the alcohols, the fractions were saponified, and after separation and purification, the alcohols converted to alcoholates. The alcoholates were filtered off from the mother liquor in vacuo, and dried on a filter paper at 60°. After 20 days, the alcoholates were almost dry, completely free from cineol. After decomposition with water, distillation with steam, and drying over sodium sulfate, 3 g of alcohol resulted:

B.p. 199-200°, d_{20}^{20} 0.9208, n_D^{20} 1.4643, $[\alpha]_D^{20}$ + 22°30'.

In its physical constants, and by the formation of phthalic acid ester, the alcohol resembled thujol most closely. The latter amount was about 20% in the indicated oil fractions of b.p. 77 to 110° (mm).

For identification of the thujol, the combined fractions were once again purified to remove of carbonyl compounds by treatment with semicarbazide, distilled with steam, oxidized with alcoholic KOH, and the thujol then converted into thujone by oxidation with chromic acid. 8 ml of thujone resulted:

B.p. 200-202°, d_{20}^{20} 0.9132, n_D^{20} 1.4506, $[\alpha]_D^{20}$ + 29.5°.

8.45 mg sub.: 24.58 mg CO_2; 8.23 mg H_2O. 9.09 mg sub.: 26.28 mg CO_2; 8.86 mg H_2O. Found %: C 79.01, 78.90; H 10.85, 10.91. $C_{10}H_{16}O$. Calculated %: C 78.89; H 10.59.

The resulting thujone was oxidized to thujoketocarboxylic acid according to the Thiemann-Semmler method [11]. The acid, thick in consistency, gave the semicarbazone, with m.p. 184° (from methyl alcohol). The 2,4-dinitrophenylhydrazone of thujone had a m.p. of 104-105°, the tribromide 120-121°.

Upon saponifying the fractions containing thujol esters, an acid was isolated whose silver salt contained 48.84% Ag. Upon analysis of the acid, % C 58.08 and H 8.71, found. The nature of the acid in question was not ascertained.

The fraction boiling at 130-142° (27 mm) contained about 60% alcohol. For identification, the fraction was

saponified, and the isolated alcohol converted to the phthalate ester. The phthalate melted at 156-160°. By saponification of the phthalate, 2.53 g of alcohol was regenerated as a viscous, slightly-dark liquid:

d_{20}^{20} 0.9300, n_D^{20} 1.505, MR_D 68.93. $C_{15}H_{26}O$. Calculated 68.68.

5.975 mg sub.: 17.605 mg CO_2; 6.283 mg H_2O. 6.535 mg sub: 19.355 mg CO_2; 6.917 mg H_2O. Found %: C 80.41, 80.82; H 12.04, 11.84; M 218.4 (according to Rast); bromine number 93.19. $C_{15}H_{26}O$. Calculated %: C 81.01; H 11.74; M 222; bromine number 97.40.

The small amount of resulting primary sesquiterpene alcohol did not permit carrying out an identification.

The oily residue remaining after isolation of the sesquiterpene alcohol indicated reaction with bromine in chloroform solution characteristic for azulogens.

Having obtained negative results upon esterification with phthalic anhydride, the authors carried out synthesis of azulene according to a method described by Kiryalov [12]. By dehydrating with 90% formic acid, the alcohol was converted into a hydrocarbon which had d_{20}^{20} 0.9123, n_D^{20} 1.4970. With solutions of bromine in acetic acid and in ethyl alcohol, the hydrocarbon became colored an intense blue-violet. The resulting hydrocarbon was dehydrogenated with metallic selenium by gentle boiling for 4 hours. The mixture was steam-distilled. From the isolated oil, azulene in the amount of 0.15 g was extracted by gasoline and 50% sulfuric acid. It was in the form of a viscous oil, indigo-blue in color, and after a double distillation with steam, was dried as an ether solution, and following removal of ether by distillation, possessed the following properties: d_{20}^{20} 0.9815, n_D^{20} 1.5810–1.5820. The picrate, prepared according to the method of Ruzicka [13], melted at 116-117°.

From the constants and from the picrate, the authors apparently synthesized azulene which approximated in structure that of chamazulene.

Ester oil after steam distillation. Upon extracting ester oil from the plant material by steam distillation, there remained 0.09% of ester oil in dissolved form in the distillation water, which the authors extracted with dichloroethane. The resulting oil, amounting to 17.3 g, had the following constants:

d_{20}^{20} 1.0112, n_D^{18} 1.4613, α_D^{20} −8°20'; acid number 235.9, ester number 29.7.

As can be seen, the oil contained a large amount of acids, 12.33% formic acid content being found in the oil according to the calomel method; isobutyric acid was found in the amount of 27.27%; it was identified by the characteristic odor and the silver salt contained 56.7% Ag. Apart from the acids, the phenols determined in the oil amounted to about 50.6%, and cineol to about 5.2%.

SUMMARY

1. By steam distillation procedure, ester oil has been obtained from above-ground portions of Zailysk wormwood Artemisia transiliensis, in 0.04% yield, and in the water left from steam distillation an additional 0.09% oil has been extracted, differing from the main product.

2. Artemisia transiliensis ester oil: a lemon-yellow liquid, cineol odor, bitter taste.

3. In the oil content there have been established the presence of: formic acid (0.01%), isobutyric acid (0.086%), m-cresol (1.5%), α-pinene (traces), cineol (55-56%), thujol (4-5%), thujol ester and an unidentified acid (6-7%), cumic aldehyde (7.5%), thujone (14-17.5%) (mixture of α- and β-forms) and a sesquiterpene alcohol (not identified).

4. The oil extracted from the waters following distillation contains: formic acid (12.33%), isobutyric acid (27.27%), phenols (56.7%) and cineol (5.2%).

5. The ester oil from the plant may find application for isolation of cineol, and use as a flotation agent.

LITERATURE CITED

[1] G. Meyer, Analysis and Determination of Organic Compounds, 1937, p. 265.

[2] A. H. Hardeing, Analyst, 39, 477 (1914).

[3] N. Ya. Demyanov and V. I. Nilov, V. V. Vilyam. Ester Oils, Their Compositions and Analysis, State Chem. Press, Moscow, 1933.

[4] Lieben, Monatsh., 14, 753 (1893).

[5] R. Shriner and R. Fuson, Systematic Qualitative Analysis of Organic Compounds, 162 (1950).

[6] Werner Bogert, J. Org. Chem., 3, 578 (1939).

[7] V. S. Johnson, et. al., Organic Reagents in Organic Analysis, Foreign Lit. Press, 60 (1950).

[8] R. G. Cooke, A. K. Macbeth, T. J. Swanson, J. Chem. Soc., 1940, 808.

[9] Bericht Schimmel, October, 1909, p. 34.

[10] Ya. B. Ashkinazi, Raw Materials in Production of Synthetic Resins, 142 (1938).

[11] Tiemann, Semmler, Ber., 30, 431 (1897).

[12] N. P. Kiryalov, J. Gen. Chem., 19, 2123 (1949).*

[13] Ruzicka, Chem. Phys. and Physik, 19 A, No. 5, 57 (1928).

Received June 19, 1954

Academy of Sciences, Kazakh SSR

* See Consultants Bureau Translation, page a-597.

INVESTIGATION OF ACONITE ALKALOIDS

III. ALKALOIDS OF THE ACONITUM ORIENTALE MILL. PLANT

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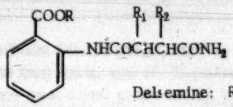
Eastern Aconite (Aconitum orientale Mill.), belonging to the Lycoctonum group, was taken as the study material in alkaloids. This large plant (height of two meters) was collected in its flowering stage in the mountain-forest zone of the Avad-khara (Georgian SSR) region, at an elevation of 1450 meters. A non-crystalline group of alkaloids (1,8%) was obtained from the roots of Aconitum orientale, from which were separated 3 alkaloids by partition of the bases according to their degree of basicity.

The first alkaloid crystallized from aqueous acetone in the form of needles containing solvent of crystallization. The substance had $[\alpha]_D$ + 44,8° (c = 2,2, chloroform). With slow heating, it lost water of crystallization, condensing at 110° and converting to a semitransparent liquid at 115-118°; the melt became transparent only at 125°. The composition of the base dried in vacuo at 110°, corresponded to the formula $C_{26}H_{31}O_{10}N_3$. Upon careful saponification of the base, an amino alcohol resulted, identical with lycoctonine, and an amino acid of m.p. 189-190°, ammonia splitting off with further saponification, forming an acid, identified as succinylanthranilic acid. Judging from the composition and character of the hydrolysis products, the alkaloid was found to be a new one, and represented a homolog of delsemine [1]; the authors propose for it the name avadkharidine (from the region in Georgia from which the plant was collected).

The structure of avadkharidine and of delsemine can be represented by the formula:



Delsemine: R_1 or R_2 = CH_3
R_1 or R_2 = H

Avadkharidine: R_1=R_2 = H

$-OR_1$ = Lycoctonine residue [2]

The second alkaloid in the base form melted at 126-128° (from heptane), $[\alpha]_D$ + 30,5° (c = 3,5, alcohol); hydrochloride m.p. 243-245°, $[\alpha]_D$ + 46,2° (c = 2,2, water). The alkaloid had a composition corresponding to the formula $C_{32}H_{41}O_9N$ An investigation of the infra-red spectrum* indicated presence of an hydroxyl group (absorption band 3560 cm^{-1}), no carbonyl or ester groups. Analytical determinations confirmed the presence of one hydroxyl only.

	Alkaloid from Aconitum orientale	Lappaconitine
Empirical formula	$C_{32}H_{44}O_9N_2$	$C_{32}H_{44}O_9N_2$
Melting point	217-218°	214°
Hydrolysis products:		
1) acid	Acetylanthranilic	Acetylanthranilic
2) amino alcohol:		
a) hydrochloride with m.p.	90-93°	93-96°
b) hydrochloride with m.p.	246-248°	246-247°
c) hydrobromide with m.p.	245-246°	240°
d) chloroaurate with m.p.	123-125°	126-127°

* Investigation of the infra-red spectrum of avadkharine was carried out in the Physical Chemistry Laboratory of the All-Union Chemico-Pharmaceutical Research Institute; it indicated the presence of absorption bands: 3560, 2960, 1470 and 1385-1400 cm^{-1}.

no alkoxyl groups being found. There was no qualitative evidence for the methyldihydroxyl group. The alkaloid was found to be a new one; the authors propose the name avadkharine.

The composition and constants for the third alkaloid, as well as the characters of its hydrolytic products, corresponded to that of lappaconitine alkaloid [3], as can be seen from the table.

It should be mentioned that during an earlier investigation of lappaconitine, synthesis of the crystalline salt failed; the base isolated by the authors from Aconitum orientale gave a readily-crystallizing hydrochloride, m.p. 207-208°, hydrobromide with m.p. 225° (with decomposition) and a perchlorate with m.p. 253° (with decomposition).

The alkaloid content in dry roots of Aconitum orientale plant, as they were investigated, was: avadkharidine 0,1%, avadkharine 0,08%, lappaconitine 0,04%. Its above-ground parts , contained 0,7% alkaloids as a non-crystallizing mixture, from which only negligible amounts of lappaconitine could be isolated.

EXPERIMENTAL

Isolation of Alkaloids from Aconitum orientale Roots

6,5 kilograms of air-dried, crushed roots was moistened with 10% ammonia and thoroughly extracted with benzene. The bases were extracted from the benzene by 10% sulfuric acid and (after alkalization of the acid extract with concentrated ammonia) with ether. There resulted 116 g of non-crystalline bases after distilling off the ether. The combined bases (116 g) were fractionated according to basicities, for which purpose they were dissolved in 410 ml of 0,5 N H_2SO_4. The aqueous solution was fractionally alkalized with 8 portions of 0,5 N NaOH (52 ml portions each time), with stirring, and in the presence of 150 ml of ether. After each addition of alkali, the aqueous solution was separated from the ether solution, and extracted twice more with ether in 150 ml portions. Upon addition of the 6th and 7th portions of alkali in the presence of ether, the avadkharidine crystalline precipitate formed, which was filtered off (3,2 g); the aqueous mother liquor was extracted with ether, as with the remaining cases. After distilling off the ether, there was obtained from the fractions 1-8 bases which did not crystallize (in the amounts, respectively, of 5, 12, 14, 15, 14, 15, 15 and 16 g). Separation of these fractions on the basis of basicities (for each, six partitions similar to that carried out on the original combined alkaloids were carried out) gave the following results: from the 2nd-5th fractions – lappaconitine (0,3, 0,4, 0,8 and 1 g), from the 7th – avadkharidine (3 g), from the 8th – avadkharine (5 g); from the 1st and 6th fractions no crystalline bases were obtained.

Avadkharidine. The base (6,2 g) was dissolved in acetone (18 ml) and the solution clarified with carbon. The addition of water (turbidity at first) caused crystallization of the base in the form of silky needles. The yield was 5,7 g. Upon slow heating, the substance contracted at 110°, melting into a semi-transparent mass at 115-118°; melt become transparent at 125°. With rapid heating, m.p. 88-91°. The crystals contained water of crystallization.

0,0670 g of the substance in 3 ml of anhydrous alcohol, $l = 0,5$, $\alpha_D + 0.50°$, $[\alpha]_D + 44,8°$. The substance which was dried at 110° in vacuo at 10 mm (where it converted into an amorphous glassy mass) was analyzed.

3,756 mg sub.: 8,602 mg CO_2; 2,509 mg H_2O. 3,720 mg sub.: 8,551 mg CO_2; 2,520 mg H_2O. 24,450 mg sub.: 1,352 ml N_2 (22°, 731 mm). 11,866 mg sub.: 0,630 ml N_2 (22°, 740 mm). Found%: C 62,50, 62,73; H 7,47, 7,58; N 6,14, 5,98. $C_{36}H_{51}O_{10}N_3$. Calculated %: C 62,9; H 7,51; N 6,13.

0,68 g of avadkharidine was dissolved in 10 ml of methanol, 2 ml of 1 N NaOH being added, and boiled for 30 minutes. After distilling off the alcohol in vacuo to a residue, water was added. Thereupon the crystalline amino alcohol separated which, after crystallization from 70% alcohol, melted at 151-153° (in vacuo); a sample mixed with lycoctonine melted at the same temperature. From the aqueous mother liquor, after separation of lycoctonine by acidification with 10% hydrochloric acid, a crystalline acid with m.p. 189-190°, precipitated. When the latter was boiled for 3 hours in aqueous solution with excess lime, ammonia split out; the excess lime was filtered off. When the aqueous mother liquor was acidified with 10% HCl solution, a crystalline acid separated, which, after crystallization from water, melted at 178-180°, and did not give depressed melting point when mixed with succinylanthranilic acid, obtained from succinic anhydride and anthranilic acid.

Avadkharine. The base (5 g) was recrystallized twice from acetone and had a m.p. of 122-124°. Recrystallization from heptane increased the m.p. to 126-128°.

0,1059 g sub. in 3,05 ml alcohol, $l = 0,5$, $\alpha_D + 0.53°$, $[\alpha]_D + 30,5°$.

3,618 mg sub.: 9,891 mg CO_2; 2,812 mg H_2O. 3,558 mg sub.: 9,730 mg CO_2; 2,861 mg H_2O. 13,662 mg sub.: 0,450 ml N_2 (22°, 731 mm). 12,751 mg sub.: 0,431 ml N_2 (24°, 763 mm). 8,537 mg sub.: 0,53 ml CH_4 (23°, 761 mm). 6,176 mg sub.: 0,38 ml CH_4 (23°, 736 mm). 10,3 mg sub.: 102 mg camphor: Δt 10,5°. Found %: C 74,60, 74,62; H 8,69, 8,99; N 3,66, 3,76; OH 4,35, 4,31. M 384. $C_{22}H_{31}O_3N$. Calculated %: C 73,9; H 8,76; N 3,92. M 358.

The avadkharine hydrochloride was prepared by the usual procedure, and recrystallized from alcohol and ether mixture, melted at 243-245°.

3.761 mg sub.: 9.270 mg CO_2; 2.748 mg H_2O. 4.329 mg sub.: 10.621 mg CO_2; 3.138 mg H_2O. 9.003 mg sub.: 0.304 ml N_2 (23°, 747 mm). 8.125 mg sub.: 2.16 ml 0.01 N H_2SO_4. Found %: C 67.26, 66.95; H 8.17, 8.11; N 3.82, 3.72. $C_{22}H_{31}O_3N \cdot HCl$. Calculated %: C 67.1; H 8.19; N 3.55.

Lappaconitine. The base (2.5 g) was recrystallized from acetone, and melted at 217-218°.

0.9036 g sub. in 10 ml $CHCl_3$, $l = 1$, $\alpha_D + 2.33°$ $[\alpha]_D + 25.8°$.

Found %: C 65.68, 65.64; H 7.68, 7.63; N 5.4. $C_{32}H_{44}O_8N_2$. Calculated %: C 65.7; H 7.59; N 4.80.

1 g of the base was dissolved in 10 ml of methanol, 1.5 ml of 40% NaOH being added, and boiled for 30 minutes. After removal of the alcohol in vacuo, water was added to the residue; in this case, crystalline amino alcohol precipitated, after which, upon crystallizing from aqueous alcohol, it melted at 90-93°. Salts were synthesized from the base (similar to those described in Schulze [3]); the hydrochloride with m.p. 246-248°, the hydrobromide with m.p. 245-246°, the chloroaurate with m.p. 123-125°. After isolation of the amino acid, the mother liquor was extracted with ether and acidified with 10 N HCl. The crystalline acid precipitated thereby, after which, crystallization from water gave a product melting at 174-175°, which did not give depression in melting point when mixed with acetylanthranilic acid.

Lappaconitine salts. The Hydrochloride. Synthesized in the form of thin needles upon addition of ether to the solution acidified with alcoholic hydrochloric acid, the base being in alcoholic solution; after crystallization from alcohol-ether mixture, the salt melted at 207-208°.

The Hydrobromide. Resulted as a crystalline precipitate when the base was ground with 5% aqueous hydrobromic acid. After recrystallization from water, the m.p. was 225.5° (with decomposition).

7.612 mg sub.: 0.275 ml N_2 (21°, 749 mm). 35.69 mg sub.: 0.520 mg H_2O (at 110° and 10 mm). Found %: N 4.13; H_2O 1.45. $C_{32}H_{44}O_8N_2 \cdot HBr \cdot 0.5H_2O$. Calculated %: N 4.16; H_2O 1.34.

The Perchlorate. Resulted in the form of an oil upon addition of an aqueous solution of magnesium perchlorate to a solution of the base in 5% HCl. Upon rubbing with a glass rod, the salt crystallized out, and after recrystallization from alcohol, melted at 253° (with decomposition).

3.200 mg sub.: 6.552 mg CO_2; 1.922 mg H_2O. 6.480 mg sub.: 0.240 ml N_2 (21°, 749 mm). Found %: C 55.87; H 6.72; N 4.39. $C_{32}H_{44}O_8N_2 \cdot HClO_4$. Calculated %: C 56.1; H 6.63; N 4.09.

Microanalytical determinations were carried out in the microanalytical laboratory of the All-Union Chemico-Pharmaceutical Research Institute, under the direction of V. V. Kolpakova.

SUMMARY

1. There have been isolated from Aconitum orientale Mill. the lappaconitine alkaloid and two new alkaloids, namely, avadkharidine and avadkharine.

2. Avadkharidine is in the form of the lycoctinine and succinylanthranilic acid ester, and thus is found to be a homolog of delsemine.

LITERATURE CITED

[1] S. Yunusov and P. K. Abubakirov, J. Gen. Chem., 21, 174, 967 (1951). *

[2] A. D. Kuzovkov, P. S. Massagetov, M. S. Rabinovich, J. Gen. Chem., 25, 157 (1955). **

[3] H. Schulze, Archiv der Pharmazie, 260, 230 (1922).

Received April 23, 1954

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* See Consultants Bureau Translation, pages 189, 1059
** " " " " " 141.

INVESTIGATION OF SCOPOLIA TANGUTICA ALKALOIDS

(SCOPOLIA TANGUTICA MAXIM.)

A. A. Ryabinin and M. N. Semenova

Up to the present time, alkaloids have been investigated in three types of Scopolia Jacq. In Scopolia japonica Maxim., were found 1-hyoscyamine, norhyoscyamine and 1-scopolamine, and in the root stock of S. carniolica Jacq., atropine, 1-hyoscyamine and scopolamine [1], and in the root stock of S. stramonifolia (Wall.) Sem. (anisodus luridus Link and Otto), there have been found 1-hyoscyamine and cuscohygrine [2]. Alkaloids of Scopolia tangutica Maxim. have not been investigated.

Scopolia tangutica is a perennial grassy plant. It was found for the first time in 1872 by the N. M. Przhevalsky expedition in the Gansu province of China, along the upper course of the Khuan-Khe (Yellow River) and its tributary, Tetung-Gol. During the second Tibet expedition of N. M. Przhevalsky, the plant was also found in North Tibet at the source of the Yan-Tse (Blue River), at an elevation of more than 3,000 meters above sea level. K. I. Maksimovich [3], a Russian botanist, described Scopolia tangutica in 1881 for the first time [3]. This new species of scopolia given to the Petersburg botanical gardens in 1884 by the Przhevalsky expedition has become acclimatized to cultivation under open soil cultivation, and has been introduced into the V. L. Komarov nursery for technical and medicinal plants of the Botanical Institute of the Academy of Sciences of the USSR. Within the short period of vegetation (June- September), the numerous grassy above-ground shoots of the Scopolia tangutica reach 1.60 meters in height, flower, and bear fruit. The root stock of Scopolia tangutica is very thick and stalky and reaches 40-50 cm in length in one-year-old specimens, with 2 cm thickness at the base.

In the present work, the authors have investigated the composition of the alkaloids in the above-ground shoots of Scopolia tangutica. The authors considered that use of above-ground parts was more advantageous than processing of the root stock. The plant was taken during the first half of June during that stage where flowering was beginning. From this plant, 2.6% mixture of bases was obtained, among them 0.40% 1-hyoscyamine, 0.26% 1-scopolamine and 0.38% (calculating as chloroaurate) of an unidentified base which was isolated as the chloroaurate with m.p. 189.5° (decomposition) and as a picrate with m.p. 201°.

EXPERIMENTAL

265 g of dry, crushed plant was moistened with aqueous ammonia solution and the alkaloids extracted by repeated chloroform extraction. From the extract which was concentrated by evaporation in vacuo, the bases were transferred to 5% sulfuric acid solution, and then after alkalization with ammonia, were again extracted with chloroform. After drying and evaporating the chloroform extract in vacuo, there was obtained 6.93 g of a mixture of bases. The alkaloids were dissolved in boiling benzene. After cooling, 1-hyoscyamine precipitated, which, after two recrystallizations, melted at 103°, yield being 1.05 g. The picrate of this alkaloid synthesized in the usual manner had a m.p. of 165°. The base and the picrate were identified with corresponding samples by the mixing test.

Found %: N 10.95. $C_{17}H_{23}O_3N \cdot C_6H_3O_7N_3$. Calculated %: N 10.81.

The benzene mother liquor was evaporated and the residue dissolved in a small amount of water. There resulted 11 ml of water extract (A). The undissolved portion was treated with a new portion of hot water, whereupon all of the bases went into solution (B). 1 ml of solution A was acidified with hydrochloric acid and precipitated with several drops of auric chloride solution. 0.092 g of chloroaurate with m.p. 184° (decomposition) precipitated. After repeated recrystallizations from boiling water this salt had a constant m.p. of 189.5° (decomposition).

Several milliliters of the solution, A, was neutralized with picric acid. The picrate which precipitated out was then recrystallized several times from boiling water, and melted at 201°. No noticeable amounts of other picrates were found upon thorough examination of the mother liquors, and it can, therefore, be considered that the picrate with m.p. 201° is a salt of the base which was separated earlier in the form of its chloroaurate.

The aqueous solution, B, was evaporated in vacuo, dissolved in alcohol, and acidified with picric acid. 1.19 g of the crude picrate of 1-scopolamine, with m.p. 181°, resulted. After several recrystallizations, the m.p. was 187.5-188°. The picrate was identified by melting of a sample mixed with the picrate of 1-scopolamine sample.

Found %: N 10.34. $C_{17}H_{21}O_4N \cdot C_6H_3O_7N_3$. Calculated %: N 10.52.

SUMMARY

0.40% of l-hyoscyamine, 0.26% l-scopolamine and 0.38% (calculating as the chloroaurate) of unidentified base have been isolated from the above ground shoots of Scopolia tangutica Maxim..

LITERATURE CITED

[1] E. Schmidt, H. Henschke, Arch. Pharm., 226, 185, 203, 214 (1888); T. Henry, The Plant Alkaloids, London (1949).

[2] C. Siebert, Arch. Pharm., 228, 145 (1890); M. S. Rabinovich and R. A. Konovalov, J. Gen. Chem., 16, 12 (1946).

[3] K. I. Maksimovich, Bull. Acad. Sci., Petersburg, 27, 508 (1881).

Received May 28, 1954

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CATALYTIC AMINATION OF ORGANIC COMPOUNDS

I. AMINATION OF ETHERS IN THE ALIPHATIC SERIES

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The amination reaction for simple ethers of the aliphatic series is not sufficiently clarified in contemporary chemistry. Thus, there exist directions to the effect that when vapors of aliphatic ethers are passed with ammonia over aluminum oxide of thorium oxide heated to 200-400°, that secondary aliphatic amines are formed [1, 2]. The catalytic amination reaction of diethyl ether was studied in the work of Opotsky and Dranovsky [3]. Alumina, silica gel, activated carbon, and copper-alumina-silica were used as catalysts. The latter catalyst was found to be the most active. A mixture of primary, secondary and tertiary amines, with a predominance of diethyl amine (up to 80%) was found as the reaction product. The yield obtained from the ether entering into reaction was related to the temperature of the reaction. Thus, at 355°, the yield of amines was 28.6%; at 365° it was 40%; at 380° it was 30%.

The reaction of ethers with aniline should be related to the same type of reaction. Thus, upon passing vapors of dimethyl ether and aniline over heated aluminum oxide, there resulted dimethylaniline [4], and from diethyl ether and aniline, in yield up to 75% of the ether entering into reaction, there was obtained diethylaniline [2].

Insufficient clarification of this reaction in the chemical literature gave grounds for Houben [5] to assert that conversion of aliphatic ethers into primary amines and alcohols, proceeding according to the equation,

$$R{-}O{-}R + NH_3 \longrightarrow RNH_2 + ROH,$$

cannot be done by any of the known methods. This situation makes inevitable a further investigation of this reaction.

In the present work, the process of catalytic amination of ethers with compressed ammonia has been studied. Selection of such conditions for carrying out this reaction, as was already proved in a work by one of us [6] earlier, is justified by the fact that the use of compressed ammonia inhibits side reactions, increasing yield of final products, and decreasing formation of unsaturated hydrocarbons, making it possible to obtain a very high yield of amines, which could not be obtained in works carried out previously.

Amination of the ethers was carried out by passing the ether vapors over heated catalyst in a stream of ammonia under 1 to 9 atmospheres pressure, at various temperatures. To carry out this process, a somewhat improved apparatus described earlier [7] was used. Aluminum oxide, silicon dioxide with aluminum oxide, thorium oxide with aluminum oxide and silica of factory brand, were used as catalysts. The best catalysts were found to be aluminum oxide, and thorium oxide with aluminum oxide. Silicon dioxide showed very little activity.

In the present work, experiments on amination of dibutyl and diisobutyl ethers have been studied. For this purpose, the ether batch was passed at a specified rate with a stream of ammonia over the heated catalyst. Depending upon the experiment, various pressures of ammonia were maintained in the apparatus, from 1 to 9 atmospheres. As the result of reaction, there was obtained in all cases liquid catalyzate in the receiver, and gas in the gas receiver. In the experiment with dibutyl ether, the gas collected was found to be butylene, and in the experiment with diisobutyl ether, isobutylene was found among the unsaturated products of reaction.

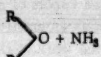
The catalyzate was treated according to the following method: it was carefully acidified, with cooling, to a weak acid reaction with hydrochloric acid solution (1:3), after which the neutral products were distilled off with steam, which, on the whole, was found to be unreacted ether. The residue in the flask was treated with alkali to a strong alkaline reaction, after which the amines were distilled with steam, and isolated from the distillate as with the neutral products, by salting out with potash, and were then analyzed, and in some cases fractionated. Upon fractionating the amines which resulted from amination of 19 g of dibutyl ether, there resulted 8.5 g of butylamine (b.p. 76-77°, d_4^{20} 0.744, n_D^{20} 1.412) and 4 g of dibutylamine (b.p. 160°, d_4^{20} 0.765, , n_D^{20} 1.422).

Upon fractionating the amines from one amination experiment, involving 19 g of diisobutyl ether, there was obtained 8 g of isobutylamine (b.p. 68-69°, d_4^{20} 0.726, n_D^{20} 1.399) along with 4.5 g of diisobutylamine (b.p. 138-139°, d_4^{20} 0.7450, n_D^{20} 1.4052.

Analysis of the amine mixture was carried out according to the methods of Mizuch and Savchenko [8]. In some cases the catalyzate consisted of two layers (oily and water layers). In a series of experiments, both layers were treated separately. From the water layer only very negligible amounts of amines were isolated; the water layer, therefore, was not treated further. The yield of amines was calculated in percentage relative to ether taken for reaction and non-reacted ether. A mixture of primary, secondary and tertiary amines resulted in all of the cases studied involving interaction of ammonia with ethers. It has been established that in the experiment with diisobutyl ether, treated beforehand with metallic sodium, isobutyl alcohol is found in the neutral reaction products.

Relative to the mechanism of amination reaction for aliphatic ethers, two directions can be hypothesized:

$$R_2O + NH_3 = RNH_2 + ROH, \quad (1)$$



$$R_2O + NH_3 = R_2NH + H_2O. \quad (2)$$

The first direction of reaction can be confirmed from the experimental data for diisobutyl ether; however, the resulting alcohol can not only be an amination product of the ether, but can also result from hydrolysis of the ether [9]. As yet no irrefutable proof exists for either mechanism of alcohol formation. Furthermore, the alcohol can undergo amination.

The formation of tertiary amines can occur as the result of modification of primary and secondary amines. As for the side reactions which lead to formation of unsaturated hydrocarbons, the following reactions can be considered:

$$(C_nH_{2n} + 1)_2O \longrightarrow 2C_nH_{2n} + H_2O,$$

$$CH_{2n} + {}_1NH_2 \longrightarrow C_nH_{2n} + NH_3,$$

$$(C_nH_{2n+1})_2NH \longrightarrow 2C_nH_{2n} + NH_3.$$

The yield of amines upon amination of ethers depends upon the conditions under which reaction proceeds, namely: the temperature, ammonia pressure, rate of ether passage over catalyst, and the nature of the catalyst. The dependence of amine yield upon temperature is presented in Table 1, from the examination of which data in the Table it can be seen that at 300° amination of ethers proceeds very slowly, and amine yield is very poor. With an increase in temperature to 370-375°, the yield of amines increases sharply. With further increase of temperature to 420°, the yield of amines again decreases sharply, but the quantity of gas increases. This is indicated by the fact that at 420° both ethers, as well as the amines which are formed, undergo decomposition with formation of butylene.

TABLE 1

Rate of Ether Passage, 20 drops per minute; ammonia pressure, 9 atms.; catalyst aluminum oxide

Quantity of dibutyl ether (g)	Temperature	Yield of amines (%)		Composition of amines (%)			Quantity of gas (liters)
		for ether taken	for reacted ether	primary	secondary	tertiary	
23.0	300°	8.8	33.6	52.3	30.2	17.5	0.5
39.0	250	27.6	67.7	58.2	31.4	10.4	2.0
36.0	370-375	47.05	65.1	54.2	35.4	10.4	3.0
23.0	420	7.9	12.1	55.6	35.3	9.1	10.0

The dependence of amine yield upon ammonia pressure is given in Table 2, from which it can be seen that in experiments carried out under a pressure of 1 atm the amine yield is very low, formation of a large amount of butylene being observed. With pressure increase, the yield of amines increases and reaches a maximum at 9 atm; at the same time the amount of butylene forming is decreased. This indicates that at a pressure of 1 atm, a large amount of ether undergoes dehydration with formation of butylene.

The dependence of amine yield upon the rate of ether passage over catalyst is given in Table 3, from which it can be seen that with increased rate of ether passage, i.e., with decreased contact time for reacting substances with the catalytic surface, the yield of amines decreases.

In order to study the effect of chemical structure for the ether upon the yield of amines, experiments were set up under identical conditions for amination of dibutyl and of diisobutyl ether.

TABLE 2

Rate of Ether Passage, 20 drops per minute

Amount of dibutyl ether (g)	Temperature	Ammonia pressure (atm)	Catalyst	Yield of amines (%)		Composition of amine (%)			Gas volume (liters)
				for ether taken	for reacted ether	primary	secondary	tertiary	
30.0	370°	1	Aluminum oxide	6.06	10.7	–	–	–	12.0
23.0	370-380	3	" "	23.2	49.5	54.2	30.3	15.5	4.0
23.0	370-380	5	" "	39.4	62.5	55.3	37.2	7.5	3.0
39.0	370-375	9	" "	45.2	60.9	52.2	35.4	12.4	4.0
35.0	370-375	1	Aluminum oxide with thorium oxide	10.95	14.2	55.0	32.3	12.7	16.0
39.0	370-380	9	The same	34.3	50.01	53.2	33.2	13.6	8.0

TABLE 3

Ammonia Pressure, 9 atm, Catalyst, Aluminum Oxide

Amount of dibutyl ether (g)	Rate of ether passage (drops per minute)	Temperature	Yield of amines (%)		Composition of amine (%)			Volume of gas (liters)
			for ether taken	for reacted ether	primary	secondary	tertiary	
19.0	10	370-380°	77.1	81.1	63.7	27.6	8.7	2.5
39.0	20	370-375	45.2	60.9	52.2	35.4	12.4	4.0

TABLE 4

Rate of Ether Passage: 10 drops per minute; Temperature, 370-375°; Ammonia Pressure, 9 atm; Catalyst, aluminum oxide

Name of ether	Quantity of ether (g)	Yield of amines (%)		Composition of amine (%)			Volume of gas (liters)
		for ether taken	for reacted ether	primary	secondary	tertiary	
Dibutyl	19.0	77.1	81.1	63.7	27.6	8.7	2.5
Diisobutyl	19.0	35.6	64.4	50.51	31.14	13.35	1.5

The results of these experiments are given in Table 4, from which it can be seen that dibutyl ether gives a higher yield of amines than does diisobutyl ether.

SUMMARY

1. A new procedure for catalytic amination of aliphatic ethers in a circulating ammonia system under pressure has been developed. Optimal conditions for the course of reaction have been established.

2. By such procedure it is possible to attain amines in yields which cannot be attained when the reaction is carried out at 1 atm of ammonia pressure.

3. The method given possesses decided advantages as compared with earlier proposed methods for amination under pressure in an autoclave, because the former ensures continuity of work, the greatest effectiveness of catalyst, and best use of reactants.

4. It has been established that the amination reaction of ethers is affected by a number of physico-chemical factors: ammonia pressure in the reaction zone, temperature, duration of contact between reactant and catalyst, nature of the catalyst, and the ether structure.

LITERATURE CITED

[1] S. Berkman, D. Morrell and G. Egloff, Catalysis in Inorganic and Organic Chemistry, State Sci.-Tech. Press, of Petroleum and Mineral Fuel Literature, II, 139 (1949).

[2] I. Houben, Methods of Organic Chemistry, IV, No. 1, Book 2, 1128 (1949).

[3] V. F. Opotsky and A. Dranovsky, Ukrain. Chem. J., 11, 446 (1936).

[4] T. H. Evans and A. N. Bourns, Can. J. Technol., 29, 1 (1950).

[5] I. Houben, Methods of Organic Chemistry, IV, No. 1, Book 1, 500 (1949).

[6] N. Kozlov and L. Akhmetshina, Proc. Acad. Sci. USSR, 35, 91 (1952).

[7] N. S. Kozlov, et. al., Symposium of the Institute of Chemistry of the BSSR, III, 5 (1937).

[8] K. G. Mizuch and A. Ya. Savchenko, Organic Chemical Industry, 7, 24 (1940).

[9] N. S, Kozlov and N. Golubovskaya, J. Gen. Chem., 6, 1506 (1936).

Received May 28, 1954

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TRICHLOROPHOSPHAZOSULFONALKYLS

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No trichlorophosphazosulfonalkyls have been known up to the present time. To obtain compounds of this type, one of the methods used for synthesis of trichlorophosphazosulfonaryls [1] was chosen, namely, reaction of phosphorus pentachloride with the corresponding sulfonic acid amides. It was found that the reaction of phosphorus pentachloride with alkylsulfonic acid amides proceeds readily in a manner similar to the scheme used for arylsulfonic acids, i.e., with the formation of trichlorophosphazosulfonalkyls:

$$AlkSO_2NH_2 + PCl_5 \longrightarrow AlkSO_2NPCl_3 + 2HCl.$$

Thus, trichlorophosphazosulfonmethyl, -ethyl, propyl, - n-butyl, -benzyl and cyclohexyl were synthesized in this manner.

The trichlorophosphazosulfonalkyls are colorless, low-melting, crystalline substances possessing a weak, characteristic odor, readily soluble in standard organic solvents, poorly soluble in petroleum ether. Using pure initial substances, the trichlorophosphazosulfonalkyls result in almost quantitative yield, and in sufficiently pure state. In the majority of cases, the "crude" substances melted in a 3° range. The trichlorophosphazosulfonalkyls are very difficult to recrystallize, because they react with moisture of the air much more rapidly than the trichlorophosphazosulfonaryls. The benzyl and cyclohexyl derivatives hydrolyze more slowly and, therefore, can be crystallized readily from petroleum ether.

The trichlorophosphazosulfonalkyls react readily with alcohols, alcoholates, phenolates, ammonia, amines, carboxylic acids, water, and other substances which contain active hydrogen. In contrast to trichlorophosphazosulfonaryls, the trichlorophosphazosulfonalkyls distill in vacuo without decomposition.

EXPERIMENTAL

0.02-0.03 mole of pulverized pure, dry amide of the corresponding alkylsulfonic acid was placed in a 50 ml round-bottomed flask, an equimolecular amount of 5% excess pure, pulverized phosphorus pentachloride added, the flask closed with an air condenser protected with a calcium chloride tube, and having mixed the reaction mixture thoroughly by hand, the mixture was heated on a water bath. Evolution of hydrogen chloride began at 45-60°, at 60-85° gas evolution became more rapid, and at 80-95° the reaction mixture became completely liquified and transparent. Hydrogen chloride evolution terminated after 15-25 minutes. After this, the reaction mixture was heated for another 30 minutes on a boiling water bath, and the flask was then immersed into the boiling water bath up to the stopper, and heating continued for 1 hour in a vacuum of 4-5 mm; thereupon, the excess phosphorus pentachloride was quantitatively distilled off and precipitated in the condenser. Trichlorophosphazo compound remained in the flask as a colorless liquid which soon crystallized completely.

Trichlorophosphazosulfonmethyl, $CH_3SO_2NPCl_3$, yield was 100%, m.p. 47-50°, crystallizing as thin needles, readily soluble in acetone, benzene, dichloroethane, ether, ethyl acetate, boiling petroleum ether; poorly soluble in cold petroleum ether.

Found %: Cl 45.14, 45.17. Eq. upon hydrolysis 4.95, 4.94. $CH_3SO_2NPCl_3$. Calculated %: Cl 46.21. Eq. upon hydrolysis 5.00.

Trichlorophosphazosulfonethyl, $C_2H_5SO_2NPCl_3$, yield 93%, m.p. 18-21°, crystallizing in needles, readily soluble in acetone, benzene, dichloroethane, ether, ethyl acetate, boiling petroleum ether; poorly soluble in cold petroleum ether.

Found %: Cl 44.14, 44.43. Eq. upon hydrolysis 5.07, 5.04. $C_2H_5SO_2NPCl_3$. Calculated %: Cl 43.57. Eq. upon hydrolysis 5.00.

Trichlorophosphazosulfonisopropyl, iso-$C_3H_7SO_2NPCl_3$, yield 100%, m.p. 19-22°, crystallizing as fine prisms, readily soluble in acetone, benzene, dichloroethane, ether, ethyl acetate, carbon tetrachloride, boiling petroleum ether; poorly soluble in cold petroleum ether.

Found %: Cl 40.84, 40.82. Eq. upon hydrolysis 5.00. $C_3H_7SO_2NPCl_3$. Calculated %: Cl 41.16. Eq. upon hydrolysis 5.00.

Trichlorophosphazosulfon-n-butyl, n-$C_4H_9SO_2NPCl_3$, yield 100%; m.p. 48-51°, crystallizing in flat needles, readily soluble in acetone, benzene, dichloroethane, ether, ethyl acetate, carbon tetrachloride, boiling petroleum ether; poorly soluble in cold petroleum ether.

Found %: Cl 40.09, 40.11. Eq. upon hydrolysis 5.03, 5.02. $C_4H_9SO_2NPCl_3$. Calculated %: Cl 39.10. Eq. upon hydrolysis 5.00.

Trichlorophosphazosulfonbenzyl, $C_6H_5CH_2SO_2NPCl_3$, yield 100%; crude substance with m.p. 77-82°, substance recrystallized from petroleum ether with m.p. 80-82° as large needles, readily soluble in acetone, benzene, boiling petroleum ether, carbon tetrachloride; poorly soluble in cold petroleum ether, carbon tetrachloride.

Found %: Cl 33.61, 33.47. Eq. upon hydrolysis 4.99, 4.98. $C_7H_7SO_2NPCl_3$. Calculated %: Cl 34.69. Eq. upon hydrolysis 5.00.

Trichlorophosphazosulfoncyclohexyl, $C_6H_{11}SO_2NPCl_3$, yield 100%; "crude" substance with m.p. 35-41°, recrystallized from petroleum ether with m.p. 39-41°, crystallizing as tablets; readily soluble in acetone, benzene, dichloroethane, ether, ethyl acetate, chloroform, carbon tetrachloride, boiling petroleum ether; poorly soluble in cold petroleum ether.

Found %: Cl 34.84, 34.71. Eq. upon hydrolysis 4.83, 4.86. $C_6H_{11}SO_2NPCl_3$. Calculated %: Cl 35.65. Eq. upon hydrolysis 5.00.

SUMMARY

Trichlorophosphazosulfonalkyls are formed in almost quantitative yields by reacting phosphorus pentachloride with alkylsulfonic acid amides.

LITERATURE CITED

[1] A. V. Kirsanov, J. Gen. Chem., 22, 269 (1952).*

Received June 3, 1954

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* See Consultants Bureau Translation, page 329.

SYNTHESIS OF DIARYLACETIC ACIDS AND THEIR ANILIDES ON THE BASIS OF DIARYLGLYCOLLIC ACID ANILIDES. XXII

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A considerable interest has been developing recently for the diarylacetic acids and their derivatives, related to the fact that some of them display herbicidal activity. For example, 4,4'-di(chlorophenyl)-acetic acid was found to be more active than 2,4-dichlorophenoxyacetic acid when tested for suppression of hypocotyls of bean plants [1]. It is known that the physiological action of the substance depends upon the position of the substituents [2]. Diarylacetic acids, containing for the most part substituents in the aromatic radicals of the acid at the para-position, have been synthesized according to procedures described in the literature [3, 4]. In order to make a thorough study of the herbicidal activity of diarylacetic acids, investigations should be carried out with all theoretically possible isomers.

The authors have undertaken the task of developing a synthetic method for diarylacetic acids on the basis of diarylglycollic acid anilides, since the latter with various substituent positions in the aromatic radicals of the acids are readily obtained by reacting organomagnesium compounds with oxanyl ether [5]. The diarylglycollic acid anilides contain mobile hydroxyl (with mineral salts they form halochromic salts [6]), and should reduce readily to diarylacetic acid anilides.

TABLE 1

Number	Heating time (hrs)	$(C_6H_5)_2CHCONHC_6H_5$ (g)	(%)	$(C_6H_5)_2CHCOOH$ (g)	(%)
1	0.3	0.54	56.8	–	–
2	0.5	0.48	50.5	0.1	15.1
3	1	0.32	33.7	0.27	40.9
4	1.5	0.22	23.2	0.35	53
5	2.5	0.14	14.7	0.46	69.7

Experiments have verified this assumption. The following were used as reducing media: Zn + CH_3COOH, $Na_2S_2O_4$, $SnCl_2$ + HCl, iodine and red phosphorus. Better results were obtained when experiments were carried out with iodine and red phosphorus in acetic acid; it was found that at the same time, along with reduction, saponification proceeded. It was important to establish the order of these reactions. For this purpose a series of experiments with benzylic acid anilide were conducted: 0.5 g iodine, 1 g of red phosphorus and 0.3 ml water were added to a solution of 1 g of the anilide in 10 ml of glacial acetic acid. Depending upon the object of the experiment, reaction mass was heated for various periods of time (Table 1).

It can be seen from the data of Table 1 that reduction and saponification proceed consecutively, and can be expressed by the scheme:

$$(C_6H_5)_2C(OH)CONHC_6H_5 \xrightarrow{H_2} (C_6H_5)_2CHCONHC_6H_5 \xrightarrow{H_2O} (C_6H_5)_2CHCOOH + C_6H_5NH_2$$

Diphenylacetic acid, or its anilide, can be obtained as the principal reaction product, depending upon the time of heating for the reaction mass.

In order to obtain the diarylacetic acids and their anilides, reaction with the anilides of diarylglycollic acids $C_6H_5NHCOC(OH)Ar_2$, where Ar = C_6H_5, o-$CH_3C_6H_4$, m-$CH_3C_6H_4$, p-$CH_3C_6H_4$, p-ClC_6H_4 and p-BrC_6H_4, was carried out. The experimental results and the properties of the resulting compound are given in Table 2.

It can be seen from the given data that to synthesize diarylacetic acid anilides, one-half hour of heating of the reaction mass is sufficient. However, more satisfactory yields of diarylacetic acids result upon heating the initial substances for 2.5-3 hours. The diarylacetic acid anilides saponify with varying ease, depending upon the position of the substituent in the aromatic radical. Thus, with 3-hour heating of the reaction mass, the yield of m,m-ditolylacetic acid amounted to 74.5%, of o,o-ditolylacetic acid 13.8%; and of p,p-ditolylacetic acid 22.1% when it was heated for 0.5 hour. The ease of saponification of the ditolylacetic acid anilides are in the order: p > m > o. As experiments by the authors have demonstrated, diarylacetic acids and their anilides can be synthesized with varying substituent positions in the aromatic radical of the acid on the basis of diarylglycollic acid anilides.

TABLE 2

Properties of Diarylacetic Acids and Their Anilides

Formula for the initial compound	Reaction products	Yield (%) heating time (hrs) 0.5	Yield (%) heating time (hrs) 2.5-3	Melting point: authors' data	Melting point: literature data
$(C_6H_5)_2C(OH)CONHC_6H_5$	$(C_6H_5)_2CHCONHC_6H_5$	–	14.7	180°	180° [7]
	$(C_6H_5)_2CHCOOH$	–	65.7	145	145-146 [10]
$(p\text{-}CH_3C_6H_4)_2C(OH)CONHC_6H_5$	$(p\text{-}CH_3C_6H_4)_2CHCONHC_6H_5$	60.5	–	166.5	–
	$(p\text{-}CH_3C_6H_4)_2CHCOOH$	22.1	–	144	144 [8]
$(m\text{-}CH_3C_6H_4)_2C(OH)CONHC_6H_5$	$(m\text{-}CH_3C_6H_4)_2CHCONHC_6H_5$	42	8.4	139-140	–
	$(m\text{-}CH_3C_6H_4)_2CHCOOH$	–	74.5	100-102	–
$(o\text{-}CH_3C_6H_4)_2C(OH)CONHC_6H_5$	$(o\text{-}CH_3C_6H_4)_2CHCONHC_6H_5$	–	51.2	171	–
	$(o\text{-}CH_3C_6H_4)_2CHCOOH$	–	13.8	155.5-157	–
$(p\text{-}BrC_6H_4)_2C(OH)CONHC_6H_5$	$(p\text{-}BrC_6H_4)_2CHCONHC_6H_5$	–	23.9	194-195.5	–
	$(p\text{-}BrC_6H_4)_2CHCOOH$	–	39	186-188	187-188 [9]
$(p\text{-}ClC_6H_4)_2C(OH)CONHC_6H_5$	$(p\text{-}ClC_6H_4)_2CHCONHC_6H_5$	–	18.6	201-205 (with decomp.)	202-204 [11]
	$(p\text{-}ClC_6H_4)_2CHCOOH$	–	52.1	166-167	166-167 [4]

EXPERIMENTAL*

Diphenylacetic acid and its anilide. 1 g of red phosphorus and 0.3 ml of water were added to a solution of 1 g benzylic acid anilide in 10 ml of glacial acetic acid and 0.5 g of iodine. The reaction mass was boiled for 2.5 hours and was then filtered into 50 ml of water containing a large amount of sodium sulfite. The resulting precipitate was filtered off and treated with 10 ml of 10% soda solution. The portion which did not dissolve was washed with water and recrystallized from alcohol. Needles with m.p. 180°. It did not give coloration with concentrated sulfuric acid. 0.14 g resulted. Diphenylacetic acid separated upon acidifying the soda filtrate with concentrated hydrochloric acid. Needles (from water) with m.p. 145°. The yield was 0.46 g. When mixed with a known sample, it did not give depression.

p,p-Ditolylacetic acid and its anilide. Initial substances: a solution of 2 g of p-tolyl acid anilide in 15 ml of glacial acetic acid, 2 g of red phosphorus, 1 g of iodine and 0.6 ml of water. Boiling time was 30 minutes. Reaction products were separated as in the preceding experiment. 1.15 g of p,p-ditolylacetic acid anilide was obtained. Needles (from glacial acetic acid) with m.p. 166.5°.

0.2174 g sub.: 7.01 ml 0.1 N H_2SO_4. 0.1931 g sub.: 6.53 ml 0.1 N H_2SO_4. Found %: N 4.51, 4.73. $C_{22}H_{21}ON$. Calculated %: N 4.44.

p,p-Ditolylacetic acid resulted in 0.32 g yield. Needles (from glacial acetic acid) with m.p. 144°.

m,m-Ditolylacetic acid and its anilide. Initial substances: a solution of 5 g of m-tolyl acid anilide in 25 ml of glacial acetic acid, 5 g of red phosphorus, 2.5 g of iodine and 1.5 ml of water. Boiling time 3 hours. 0.4 g of m,m-tolylacetic acid anilide was obtained. Needles grouped in nodules, with m.p. 139-140°. The anilide was poorly soluble in gasoline and dissolved readily in other solvents.

0.0925 g sub.: 5.8 ml 0.05 N H_2SO_4. Found %: N 4.38. $C_{22}H_{21}ON$. Calculated %: N 4.44.

m,m-Ditolylacetic acid resulted in 2.7 g yield. Needles (from dilute acetic acid) with m.p. 100-102°. The acid dissolved in standard organic solvents.

0.1060 g sub.: 0.3098 g CO_2; 0.0646 g H_2O. Found %: C 79.76; H 6.82. $C_{16}H_{16}O_2$. Calculated %: C 80.00; H 6.67.

In the experiment with 1 g of m-tolyl acid anilide (heating time 30 minutes), 0.4 g of m,m-ditolylacetic acid anilide resulted, M.p. was 139-140°.

o,o-Ditolylacetic acid and its anilide. The reaction mass, consisting of 7 g of o-tolyl acid anilide in 35 ml of glacial acetic acid, 3.5 g of iodine, 7 g of red phosphorus and 2.5 ml of water, was boiled for 3 hours. o,o-Ditolylacetic acid does not dissolve in gasoline, but dissolves well in other organic solvents. Needles (from alcohol)

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with m.p. 171°; 3.4 g was obtained.

0.2180 g sub.: 0.6680 g CO_2; 0.1320 g H_2O. 0.2028 g sub.: 0.6206 g CO_2; 0.1232 g H_2O. 0.2174 g sub.: 7.01 ml 0.1 N H_2SO_4. 0.1931 g sub.: 6.49 ml 0.1 N H_2SO_4. Found %: C 83.62, 83.51; H 6.78, 6.79; N 4.51, 4.70. $C_{22}H_{21}ON$. Calculated %: C 83.81; H 6.67; N 4.44.

o,o-Ditolylacetic acid crystallized as needles from glacial acetic acid. M.p. 155.5-157°. Yield was 0.7 g.

0.2612 g sub.: 0.7623 g CO_2; 0.1564 g H_2O. 0.2330 g sub.: 0.6816 g CO_2; 0.1402 g H_2O. Found %: C 79.83, 79.82; H 6.71, 6.73. $C_{16}H_{16}O_2$. Calculated %: C 80.00; H 6.67.

4,4'-Di-(bromophenyl)-acetic acid and its anilide. Initial substances: a solution of 4 g of 4,4'-di-(bromophenyl)-glycollic acid anilide in 40 ml of glacial acetic acid, 2 g of iodine, 4 g of red phosphorus and 1.2 ml of water. Boiling time was 2.5 hours. There resulted 0.92 g of 4,4'-di-(bromophenyl)-acetic acid anilide. Needles with m.p. 194-195.5°. The anilide did not dissolve in water or gasoline; it dissolved readily in alcohol, benzene and acetic acid.

0.1098 g sub.: 4.95 ml 0.05 N H_2SO_4. 0.1150 g sub.: 5.03 ml 0.05 N H_2SO_4. Found %: N 3.16, 3.06. $C_{20}H_{15}ONBr_2$. Calculated %: N 3.14.

4,4'-Di-(bromophenyl)-acetic acid resulted in 1.25 g yield. M.p. 186-188°.

4,4'-Di-(chlorophenyl)-acetic acid and its anilide. For reaction there were taken: a solution of 1.4 g of 4,4'-dichlorobenzylic acid anilide in 12 ml of glacial acetic acid, 1.4 g of red phosphorus, 0.7 g of iodine and 0.4 ml of water. The boiling time was 3 hours. 0.25 g of 4,4'-di-(chlorophenyl)-acetic acid anilide was obtained. Needles (from alcohol) with m.p. 201-205° (with decomposition).

0.1150 g sub.: 6.6 ml 0.05 N H_2SO_4. 0.1532 g sub.: 8.7 ml 0.05 N H_2SO_4. Found %: N 4.02, 3.98. $C_{26}H_{15}ONCl_2$. Calculated %: N 3.93.

0.55 g of 4,4'-di-(chlorophenyl)-acetic acid was isolated. M.p. 166-167°.

SUMMARY

1. A preparational procedure has been developed for synthesizing diarylacetic acids and their anilides, based upon that for diarylglycollic acid anilides. This procedure makes it possible to synthesize diarylacetic acids and their anilides with various positions of the substituents in the aromatic ring of the acid.

2. It has been found that, depending upon the position of the substituents in the radicals of the acid, the ease of saponification of diarylacetic acid anilides proceeds in the order: p > m > o.

3. m,m-Ditolyl- and o,o-ditolylacetic acids and their anilides, as well as p,p-ditolyl- and 4,4'-di-(bromophenyl)-acetic acid anilides, not described in the literature, have been synthesized, and their properties studied. The substances obtained may be of interest in connection with the display of herbicidal activity for a given group of the compounds.

LITERATURE CITED

[1] J. Casidu and T. Allen, Science, 113, 553 (1951).

[2] N. N. Melnikov and Yu. A. Baskakov, Prog. Chem., 23, 157 (1954).

[3] Beilst., IX, 673.

[4] Synthesis of Organic Compounds, Foreign Lit. Press, 4, 234 (1953).

[5] P. A. Petyunin and N. G. Panferova, J. Gen. Chem., 17, 502 (1947).

[6] P. A. Petyunin and I. S. Berdinsky, J. Gen. Chem., 21, 1704 (1951).*

[7] Beilst., XII, 280.

[8] Fritsch and Feldmann, Ann., 306, 81 (1899).

[9] Biltz, Ber., 43, 1819 (1910).

[10] R. F. Reeves and H. G. Lindvoll, J. Am. Chem. Soc., 64, 1089 (1942).

[11] K. Gätzi and W. Stambach, Chem. Abs., 1946, 5040.

Received June 23, 1954

Molotov Institute of Pharmacy

* See Consultants Bureau Translation, page 1877.

CHEMICAL STRUCTURE AND PARASITICIDAL ACTIVITY

XIV. ACRIDINE COMPOUNDS WITH CYCLIC SIDE SUBSTITUENTS ADDED TO THE RING VIA THE NH-GROUP

V. I. Stavrovskaya

Soviet synthetic preparations – atebrin, plasmocide and recently bigumal – have played an outstanding role in therapeutic and prophylactic use in the fight against malaria. However, a shortage of prophylactic substances with prolonged action, and of preparations specific for tissue forms of the parasite, the high toxicity of plasmocide, and the undue number of relapses during atebrine therapy, pose for the chemists a problem of synthesizing better preparations for effecting the germicidal effect.

A search for more effective antimalarial substances within the acridine and quinoline series, with compounds containing a side substituent designed according to a new type, was carried out by the author. The distinctive, structural peculiarity for a large number of anti-malarial compounds of the quinoline and acridine series, is the presence of aliphatic dialkylaminoalkyl side groups – or "chains" – connected to the acridine or quinoline nucleus by the NH-group. This "chain" character for the side group, the structural details of which are modified, has continued to be one of the most important salient principles in the task of creating new anti-malarial compounds for the twenty-year period starting from the appearance of the first synthetic anti-malarial preparation (plasmochin in 1926).

The author maintains that aliphatic dialkylaminoalkyl amines can be substituted by aromatic amines of known structure and distribution of substituents. Aminobenzylethyl amines, and their substituted derivatives, were used for such amines.

The possibilities for substitution of aliphatic diamines by aromatic amines in anti-malarial compounds of the acridine and quinoline series offers a wide range of variation in substituents, their number, and position in the benzene nucleus, for purposes of increasing preparation potency.

First syntheses of anti-malarial substances with cyclic side chains were carried out by the author for the acridine series. To clarify the author's assumption concerning the possibility of appearance of anti-malarial activity in compounds of this series when aromatic amines of specific structure are introduced as side chains, 2-methoxy-6-chloro-9-aminoacridine derivatives were synthesized, in the 9-position of which were placed the o-, m- and p-aminobenzyldiethylamine radicals (Tables 3, 2, 1). Tests with avian malaria have demonstrated that the compounds synthesized possess anti-malarial activity, and better activity was found with 2-methoxy-6-chloro-9-(3'-diethylaminomethylphenyl)-aminoacridine (No. 2).*

According to the literature data, 2-methoxy-6-chloro-9(phenyl)-aminoacridine, which in structure superficially resembles the first three compounds, differing from them only in lacking a diethylaminomethyl group, showed very low anti-malarial activity (Q 0.04) [3].

In addition, hydroxy and methoxy groups were introduced into the most active compound (No. 2) in a position para- to the NH-group. The author synthesized 2-methoxy-6-chloro-9-(3'-diethylaminomethyl-4'-hydroxyphenyl)-aminoacridine (No. 5) and 2-methoxy-6-chloro-9-(3'-diethylaminomethyl-4-methoxyphenyl)-aminoacridine (No. 6).** To increase the potency of preparation No. 5, a second diethylaminomethyl was introduced in the position ortho- to the hydroxyl and meta- to the NH-group. For this purpose, 2-methoxy-6-chloro-9-[3',5'-bis-(diethylaminomethyl)-4'-hydroxyphenyl]-aminoacridine (No. 7) was synthesized.

In addition to the above-described compounds, two preparations were synthesized with cyclic side chains, obtained by synthesis of 2-hydroxy-5-nitrobenzyldiethylamine [5, 6], and their structures determined: namely, 2-methoxy-6-chloro-9-(3'-diethylaminomethylsaligeninmethylenic ester)-aminoacridine (No. 8) and 2-methoxy-6-chloro-9-[(3'-diethylaminomethyl-4'-hydroxy-5'-hydroxymethyl)-phenyl]-aminoacridine (No. 9).

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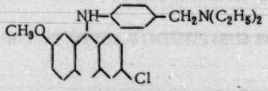
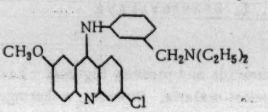
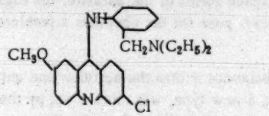
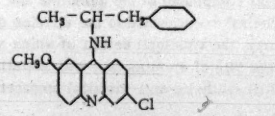
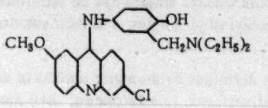
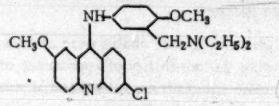
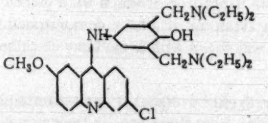
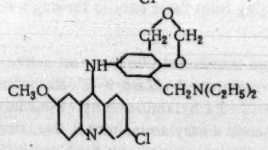
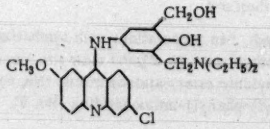
* After the above-enumerated preparations had been synthesized by the author and tested on avian malaria, there appeared a work by Hall and Turner [1], wherein one of the synthesized compounds was described, namely, 2-methoxy-6-chloro-9-(2'-diethylaminomethylphenyl)-aminoacridine. Later (in the year 1947), an American patent was published in which all three of the acridine preparations synthesized by the present author were mentioned [2].

** Compounds analogous to preparations No. 5 and 6 were later described in a work by Burckhalter [4].

Number	Formula	Melting point	
		Bases	Hydrochloride
1			227-228°
2		107-108°	253-254
3			210-211
4			199-200
5		175	179-180 (decomposition)
6		98-100	201-202
7		143-144	233-236 (decomposition)
8		113-114	Above 270°
9			Picrate 174-176 (decomposition)

Synthesis of acridine compounds with cyclic side chains was carried out in three different ways: 1) by the standard procedure in phenol medium, 2) by 2-hour heating with a weakly acid solution of 2-methoxy-6,9-dichloroacridine and the corresponding aromatic amine, and 3) according to the Mannich reaction, from 2-methoxy-6-chloro-9-(4'-hydroxyphenyl)-aminoacridine, formaldehyde and diethylamine [7].

The most general and convenient was found to be the second method -- heating of 9-chloroacridines with aromatic amines in weakly acid medium. The resulting products are pure and result in good yields. Some of them, after cooling of the reaction mass, precipitated in the form of hydrochlorides.

The bases of synthesized acridine compounds were solid substances, colored from light yellow to orange color. The hydrochlorides, as a rule, were or orange-red color.

All of the compounds synthesized were found to be effective when tested for P. relictum on finches and linnets. According to the degree of anti-malarial potency* the compounds synthesized can be arranged in the following order: preparation No. 7 is approximately three-fold more active than atebrin, and its toxicity is lower than that of atebrin; preparation No. 5 is 2-fold more active than atebrin and its toxicity less than that of atebrin; preparations Nos. 6 and 9 are approximately of the same activity as atebrin, toxicity being lower than that of the latter, and preparations Nos. 8, 3 and 1 are lesser in activity than atebrin and their toxicity is also less than that of atebrin.

Thus, upon replacing the aliphatic side "chain" in acridine compounds by aminobenzyldiethylamines and their substituted derivatives, there are formed anti-malarial substances of schizotropic action, with activity resembling that of atebrin, and in some cases surpassing the latter several-fold, with toxicity less than that of atebrin. Anti-malarial activity is clearly exhibited with m-aminobenzyldiethylamine present as a side chain; methoxy and hydroxy groups introduced into a para-position to the NH-group increase considerably this activity; the introduction of a second diethylaminomethyl group improves several-fold the anti-malarial activity.

The author wishes to express her appreciation to Sh. D. Moshkovsky and S. A. Syrkina for carrying out the biological tests.

EXPERIMENTAL

2-Methoxy-6-chloro-9-(3'-diethylaminomethylphenyl)-aminoacridine. Synthesized by standard procedure from 2-methoxy-6,9-dichloroacridine and m-aminobenzyldiethylamine in phenol medium. After termination of reaction, the liquid mixture was poured into ether, and the thick oil which precipitated was washed once with ether. The resulting viscous orange mass solidified when treated with concentrated hydrochloric acid. The product was ground and shaken repeatedly with fresh portions of acetone. It was crystallized from alcohol, platelets, orange in color, m.p. 252-253°.** The hydrochloride was readily soluble in water and alcohol.

3.770 mg sub.: 0.279 ml N_2 (20°, 741 mm). 4.260 mg sub.: 0.318 ml N_2 (22°, 734 mm). Found %: N 8.41, 8.34. $C_{25}H_{28}ON_3Cl_2$. Calculated %: N 8.53.

The base, bright yellow in color, crystallized from acetone. Platelets, m.p. 107-108°.

3.899 mg sub.: 0.353 ml N_2 (23°, 743 mm). 3.373 mg sub.: 0.304 ml N_2 (23°, 743 mm). Found %: N 10.21, 10.16. $C_{25}H_{29}ON_3Cl$. Calculated %: N 10.01.

2-Methoxy-6-chloro-9-(2'-diethylaminomethylphenyl)-aminoacridine (No. 2). Obtained by the usual procedure in phenol medium; treatment of the reaction product was the same as for the corresponding m-isomer. The hydrochloride was yellow in color, crystallizing from anhydrous alcohol with ether. M.p. 210-211°. Less soluble in water than the m-isomer; soluble in alcohol.

5.160 mg sub.: 0.436 ml N_2 (21°, 733 mm). 3.850 mg sub.: 0.328 ml N_2 (22°, 734 mm). Found %: N 9.46, 9.62. $C_{25}H_{27}ON_3Cl_2$. Calculated %: N 9.21.

2-Methoxy-6-chloro-9-(4'-diethylaminomethylphenyl)-aminoacridine (No. 1). Synthesized by the usual method in phenol medium. The hydrochloride was crystallized from alcohol in the form of platelets, orange in color. M.p. 263-265°.

8.448 mg sub.: 0.618 ml N_2 (20°, 753 mm). 6.874 mg sub.: 0.490 ml N_2 (20°, 752 mm). Found %: N 8.44, 8.22. $C_{25}H_{28}ON_3Cl_2$. Calculated %: N 8.53.

* The activity of the preparation was determined by its ability to cause retardation in appearance of parasites in the blood as compared with the control, when introduced for 5 days in succession from time of infection.

** The indicated m.p. for the dihydrochloride of 2-methoxy-6-chloro-9-(3'-diethylaminoethylphenyl)-aminoacridine was 278° [3]; in the author's experiments, this compound melted at 252-253°.

2-Methoxy-6-chloro-9-(β-phenyl-α-methylethyl)-aminoacridine. Synthesized in the usual fashion in phenol medium. Yellow color. Melting point of the hydrochloride was 199-200°. The product was poorly soluble in water, soluble in alcohol.

3.320 mg sub.: 0.213 ml N_2 (20°, 726 mm). 3.070 mg sub.: 0.193 ml N_2 (22°, 726 mm). Found %: N 7.14, 6.95. $C_{23}H_{22}ON_2Cl_2$. Calculated %: N 6.78.

2-Methoxy-6-chloro-9-(3'-diethylaminomethyl-4'-hydroxyphenyl)-aminoacridine (No. 5). 2-Hydroxy-5-acetaminobenzyldiethylamine (23.6 g) was boiled with 50 ml of 20% hydrochloric acid for 1 hour. The cooled liquid was neutralized with a 40% solution of caustic soda and then with 2-3 drops of concentrated hydrochloric acid, acidified to an acid reaction for Congo red. The 2-methoxy-6,9-dichloroacridine (27.8 g) was poured into a flask and the reaction mixture heated on a boiling water bath for 2 hours with stirring. At the end of the heating, the flask contents were in the form of a thick orange-red gruel. The solid substance was filtered off and washed with acetone; amount was 48 g.

The product was dissolved, with heating, in 400 ml of water, to which was added 40 ml of 10% hydrochloric acid, and filtered off from the insoluble particles. After cooling, the hydrochloride precipitated in the form of orange-red colored, small needles. The yield was 36 g (82%). M.p. was 179-180° (decomposition). The hydrochloride was soluble in water and alcohol.

5.470 mg sub.: 0.372 ml N_2 (23°, 743 mm). 7.466 mg sub.: 0.490 ml N_2 (24°, 746 mm). Found %: N 7.67, 7.40. $C_{25}H_{28}O_2N_3Cl_3 \cdot 2H_2O$. Calculated %: N 7.71.

The base, orange-colored needles with m.p. 175°, was readily soluble in alcohol, acetone and benzene, soluble in ether and petroleum ether, and insoluble in water. It crystallized from petroleum ether.

6.672 mg sub.: 0.568 ml N_2 (23°, 751 mm). Found %: N 9.70. $C_{25}H_{28}O_2N_3Cl$. Calculated %: N 9.64.

2-Methoxy-6-chloro-9-(3'-diethylaminomethyl-4'-methoxyphenyl)-aminoacridine (No. 6). Synthesized by the usual manner in phenol medium from 2-methoxy-6,9-dichloroacridine (2.8 g) and 3-diethylaminomethyl-4-methoxyaniline (2.1 g). The yield was 4.3 g (95%). The orange-yellow base crystallized from aqueous acetone. Small prisms with m.p. 98-100°. Very soluble in alcohol, acetone, benzene and ether; soluble in dilute acids; insoluble in water.

3.760 mg sub.: 0.323 ml N_2 (29°, 749 mm). 4.231 mg sub.: 0.353 ml N_2 (29°, 749 mm). Found %: N 9.57, 9.29. $C_{26}H_{28}O_2N_3Cl$. Calculated %: N 9.34.

The hydrochloride was red-orange in color, crystallized from alcohol-ether, and the m.p. was 201-202°. Readily soluble in water and alcohol.

4.844 mg sub.: 0.333 ml N_2 (30°, 752 mm). 2.772 mg sub.: 0.196 ml N_2 (30°, 752 mm). Found %: N 7.66, 7.88. $C_{26}H_{30}O_2N_3Cl_3 \cdot 2H_2O$. Calculated %: N 7.52.

2-Methoxy-6-chloro-9-[3',5'-bis-(diethylaminomethyl)-4'-hydroxyphenyl]-aminoacridine (No. 7). 3,5-bis-(Diethylaminomethyl)-4-hydroxyacetanilide (6.4 g) was boiled with 10 ml of 20% hydrochloric acid for 1 hour. The cooled liquid was neutralized with 40% sodium hydroxide solution, and then acidified with concentrated hydrochloric acid to a weak acid reaction. 2-Methoxy-6,9-dichloroacridine (5.6 g) was placed in the flask and the reaction mixture heated on a boiling water bath with stirring for 2 hours. The resulting red hydrochloride (10.2 g) was filtered off and dried. When the aqueous hydrochloride solution was alkalinized with potash, an orange-colored base separated. It was crystallized from a mixture of petroleum ether and benzene. M.p. was 143-144°.

5.658 mg sub.: 0.510 ml N_2 (20°, 762 mm). 5.479 mg sub.: 0.510 ml N_2 (22°, 760 mm). Found %: N 10.53, 10.77. $C_{30}H_{37}O_2N_4Cl$. Calculated %: N 10.76.

The bright-red-colored hydrochloride was readily soluble in water. M.p. was 233-235° (decomposition).

5.180 mg sub.: 0.392 ml N_2 (23°, 748 mm). 4.671 mg sub.: 0.353 ml N_2 (24°, 748 mm). Found %: N 8.59, 8.55. $C_{30}H_{48}O_2N_4Cl_4 \cdot H_2O$. Calculated %: N 8.64.

2-Methoxy-6-chloro-9-[3',5'-bis-(diethylaminomethyl)-4'-hydroxyphenyl]-aminoacridine and 2-methoxy-6-chloro-9-(3'-diethylaminomethyl-4'-hydroxyphenyl)-aminoacridine. 2-Methoxy-6-chloro-9-(4'-hydroxyl)-aminoacridine (7 g), formalin (4 ml), diethylamine (15 ml) and alcohol (100 ml) were heated on a water bath for 11 hours, with stirring. After termination of the heating, the dark-red solution was filtered off from a small amount of 2-methoxy-6-chloro-9-(4'-hydroxyphenyl)-aminoacridine. Alcohol and diethylamine were distilled off, and the resulting mixture was dissolved in ether, whereupon a portion of the material (1.6 g) did not dissolve in the ether and was filtered off. The ether solution was dried with potash. After distilling off the solvent, the remaining dark-red

viscous mass was once again dissolved in ether, and in this case not very much of the substance dissolved in the ether, and was filtered off (0.3 g). This operation of dissolving in ether was repeated several times to the complete removal of ether-insoluble material, portions of which were collected and crystallized from petroleum ether; m.p. 174-175°. A sample mixed with 2-methoxy-6-chloro-9-(3'-diethylaminomethyl-4-hydroxyphenyl)-aminoacridine synthesized by the above-described procedure, did not produce depression in melting point. The residue, after distilling off the ether, crystallized from a mixture of benzene and petroleum ether; m.p. was 143-144°. A sample mixed with 2-methoxy-6-chloro-9-[3',5'-bis-(diethylaminomethyl)-4'-hydroxyphenyl]-aminoacridine did not give depression.

2-Methoxy-6-chloro-9-(3'-diethylaminomethylsaligeninmethylene ester)-aminoacridine (No. 8). Obtained from 3-diethylaminomethyl-5-aminosaligeninmethylene ester (1.5 g) and 2-methoxy-6,9-dichloroacridine (1.75 g) in weakly alkaline medium. Quantity of base obtained was 2.4 g (80%). The base, yellow in color, crystallized from aqueous acetone or benzene. Small prisms, with m.p. 113-114°. Soluble in alcohol, acetone and benzene.

3.957 mg sub.: 0.323 ml N_2 (28°, 744 mm). 3.436 mg sub.: 0.284 ml N_2 (28°, 744 mm). Found %: N 9.06, 9.17. $C_{27}H_{28}O_3N_3Cl$. Calculated %: N 8.80.

Hydrochloride, red in color, melted above 270°.

4.630 mg sub.: 0.304 ml N_2 (29°, 744 mm). 3.919 mg sub.: 0.265 ml N_2 (28°, 744 mm). Found %: N 7.26, 7.50. $C_{27}H_{30}O_3N_3Cl_3 \cdot H_2O$. Calculated %: N 7.39.

2-Methoxy-6-chloro-9-(5'-diethylaminomethyl-4'-hydroxy-5'-hydroxymethylphenyl)-aminoacridine (No. 9). Obtained by heating 2-methoxy-6,9-dichloroacridine (2.8 g) for 2 hours on a boiling water bath with 2-hydroxy-3-diethylaminomethyl-5-aminobenzyl alcohol in weakly acid medium. The reaction product was dissolved in water while boiling, filtered off and alkalized with aqueous ammonia. A picrate was obtained from the base, which, when crystallized from alcohol, melted at 174-176° (decomposition).

2.814 mg sub.: 0.333 ml N_2 (22°, 755 mm). 3.056 mg sub.: 0.363 ml N_2 (21°, 754 mm). Found %: N 13.60, 13.68. $C_{38}H_{34}O_{17}N_9Cl$. Calculated %: N 13.64.

SUMMARY

1. A number of acridine compounds with cyclic side chains, aminobenzyldiethylamines and their derivatives, substituted in the nucleus at the 9-position through the NH-group, have been synthesized and characterized.

2. Replacement of the aliphatic diamine in acridine compounds by aminobenzyldiethylamines and their substitution products results in anti-malarial compounds of schizotropic activity, whose toxicity is less than that for atebrin; the activity approximates that of atebrin, in some cases exceeding the latter by 2-3 fold (Nos. 5, 7).

3. Anti-malarial activity is clearly apparent with m-aminobenzyldiethylamine as the side chain; introduction of the hydroxy and methoxy groups in para-position to the NH-group, increases considerably the anti-malarial activity; introduction of a second diethylaminomethyl in a meta-position to the NH-group increases somewhat the anti-malarial activity.

LITERATURE CITED

[1] D. M. Hall, E. E. Turner, J. Chem. Soc., 1945, 694.

[2] F. Wiselogle. A Survey of Antimalarial Drugs (1946).

[3] J. H. Burckhalter, A. L. Rawlins, et. al., U. S. Patent 2,419,199 (1947).

[4] J. H. Burckhalter, F. H. Tendic, et. al., J. Am. Chem. Soc., 70, 1363 (1948).

[5] V. I. Starovskaya and K. S. Topchiev, J. Gen. Chem., 21, 525 (1951).*

[6] V. I. Stavrovskaya, J. Gen. Chem., 24, 2068 (1954).*

[7] J. H. Burckhalter, H. de Wald, et. al., J. Am. Chem. Soc., 72, 1024 (1950).

Received May 25, 1954

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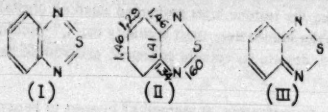
* See Consultants Bureau Translation, page 581.

" " " " "

THE STRUCTURE AND SOME PROPERTIES OF PIAZOTHIOLE

L. S. Efros and R. M. Levit

Until very recently, structure (I) was attributed to the product, piazothiole, obtained by condensation of o-phenylenediamine with sulfur dioxide [1], or with thionyl chloride [2], based upon methods of synthesis. However, measurements of inter-atomic distances [3], the results of which are given in (II), have indicated clearly that the sulfur atom in piazothiole is divalent, and that the benzene ring has a quinoid structure as indicated in Formula (III):



(I) (II) (III)

Thus, closing of the thiodiazole ring provokes considerable rearrangement of the π-electron cloud for the entire molecule, in which this phenomenon surpasses in all respects that observed for benzimidazole [4] and benztriazole [5].

The purpose of the present work was a study of certain properties of piazothiole and its simplest derivatives in order to attempt, by chemical methods, to confirm the correctness for a quinoid formula of structure (III) as given above.

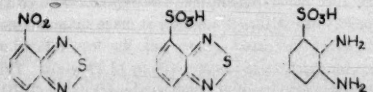
According to the known Fries rule concerning lower stability of quinoid structures as compared with benzenoid [6], it was to be expected that piazothiole would have unsaturated properties so characteristic for quinones. However, piazothiole, as the authors' experiments indicate, does not decolorize bromine water, does not react with halogens in the absence of catalysts, and does not give addition products with substances of the H—A type. Its only characteristic reaction as a quinone derivative is reduction in acid medium, wherein opening of the heterocyclic ring occurs with formation of o-phenylenediamine and hydrogen sulfide. This reaction is found to be a convenient procedure for determination of the structure of certain piazothiole derivatives, and in some cases, a good preparative method for synthesis of substituted o-phenylenediamine [7].

The substitution reaction was found to be most characteristic for piazothiole. It follows from Formula (III) that heterocyclic nitrogen atoms should pull electrons away from the benzene ring, making it less reactive with respect to electrophilic reagents, and where reactivity of positions 5 and 6 conjugated with hetero atoms should be weakened in particular.

Thus, it follows from the above that electrophilic substituents should enter the piazothiole molecule most readily at positions 4 and 7.

Indeed, it was demonstrated earlier [7], that upon nitration of piazothiole, contrary to the literature data [8], there is formed 4-nitropiazothiole (IV), whose structure has been accurately proved both by synthesis from 3-nitro-1,2-phenylenediamine and thionyl chloride, and by reduction rupture, where triaminobenzene* is formed.

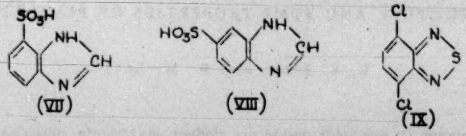
Sulfonation of piazothiole can be carried out only under quite rigid conditions, at 150-160°, using oleum, in which case the monosulfonic acid results in good yield (V):



(IV) (V) (VI)

* The authors learned recently that 4-nitropiazothiole has also been synthesized by L. Peyron (see Bull. Soc. Chim., 1948, 502).

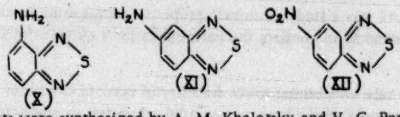
Its structure was proved by reduction rupture, wherein 1,2-phenylenediamine-3-sulfonic acid (VI) was obtained, which was converted, when reacted with formic acid, into the 4-sulfonic acid of benzimidazole (VII), differing in properties from the 5-sulfonic acid of benzimidazole (VIII) which was described by one of us [9].



(VII) (VIII) (IX)

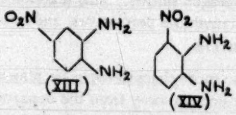
Chlorination of piazothiole proceeded only when chlorine was passed through the melted product in the presence of iron shavings. Reaction does not proceed in the absence of catalyst. By controlling the course of this reaction from the weight increase, calculated on the basis of monochloro derivative formation, the authors obtained a non-crystallizable oil which distilled in high vacuum. Thereupon, it was possible to isolate about one-half of the original piazothiole taken for reaction, the residue after prolonged standing crystallizing out. Analysis indicated that the resulting product was the dichloroderivative, most probably the 4,7-dichloropiazothiole (IX). Thus, during nitration, sulfonation and chlorination, despite its quinoid structure, piazothiole behaves in a manner similar to that for normal aromatic compounds.

As a further development of the investigation, it seemed of interest to become acquainted with the properties of the isomeric 4-amino-(X) and 5-amino-(XI)-piazothioles.



(X) (XI) (XII)

Both of these products were synthesized by A. M. Khaletsky and V. G. Pesin [8, 10] before us, by reduction of the corresponding nitro derivatives (IV) and(XII); in this case 4-nitropiazothiole (IV), as was already indicated, is readily synthesized by direct nitration of piazothiole, while its isomer, 5-nitropiazothiole (XII) can be obtained by condensation of 4-nitro-1,2-phenylenediamine (XIII) with thionyl chloride [8].



(XIII) (XIV)

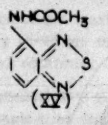
In the preceding article [7], in attempting to synthesize compound (XII) by this procedure, the authors pointed out that compared with o-phenylenediamine and 3-nitro-phenylenediamine (XIV), the 4-nitro-1,2-phenylenediamine (XIII) does not readily enter into reaction, and this fact was explained by the electrophilic effect of the nitro group in position 4, inhibiting rearrangement of the π-electron cloud of the molecule which is necessary for closure of the thiodiazole ring.

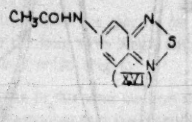
In the experimental part of the work, the authors also gave data attesting to the fact that according to the directions of A. M. Khaletsky and V. G. Pesin [8], 5-nitropiazothiole(XII) fails to separate from the reaction products. Apparently having neglected to scrutinize the details, the above-mentioned authors in their preceding work [10], attributed to us, without grounds, the statement that 4-nitro-1,2-phenylenediamine (XIII) cannot, on the whole, be condensed with thionyl chloride, and even the statement that 5-nitropiazothiole (XII) cannot exist, as though in accordance with the theory developed by us. Although we did not make these unusual assertions [7], as can be clearly seen from the preceding, the above-indicated authors, non-the-less, refuted our non-existent assertions by describing a new synthetic procedure for the 5-nitro isomer (XII) in 18.2% yield. This yield, indeed, confirms correctly our assertion concerning lower reactivity of 4-nitrophenylenediamine (XIII) as compared with o-phenylenediamine and 3-nitrophenylenediamine (XIV), from which the piazothiole derivatives were obtained by us under identical conditions in 90 and 70% yields.

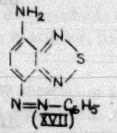
In the present work, having carried out condensation of 4-nitrophenylenediamine (XIII) with thionyl chloride under more rigorous conditions, and using superheated steam distillation for isolation of 5-nitropiazothiole, the authors were able to increase the yield of this product to 75%. The synthetic procedures for 4-amino- and 5-aminopiazothiole, from their nitro derivatives, were considerably modified and improved by the authors as well.

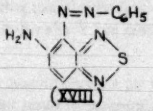
Both amines were moderately soluble in water, intensely-colored green-yellow, long, light needles; 4-amino piazothiole, in distinction to the isomer (XI), fluoresces brightly with a green light during ultraviolet exposure. Both amines were found to be relatively weak bases: the basicity constants for both isomers, calculated by the authors according to potentiometric titration data for the products (see experimental) were equal to the value $10^{-11.3}$. The intense color and low basicity of the amine speak in favor of the correctness of the quinoid structure.

At the same time, 4-aminopiazothiole (X) and 5-aminopiazothiole (XI) entered into all reactions characteristic for aromatic amines. Thus, when reacted with acetic anhydride, they formed readily the corresponding acetyl derivatives (XV) and (XVI), of which (XV) fluoresced with a bluish light brightly upon exposure to ultra-violet light. Both amines enter very readily into azo coupling with diazo compounds. The products resulting upon coupling with diazotized aniline (XVII) and (XVIII) were purified and analyzed by the authors.


(XV)


(XVI)

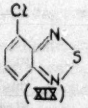

(XVII)

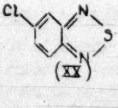

(XVIII)

The p-aminoazo dye (XVII) forms salts readily with mineral acids, which are more deeply colored than the base. The ortho-isomer (XVIII) does not form salts with acids as do the majority of o-aminoazo compounds. Reduction of the azo groups of these substances proceeds with simultaneous opening of the thiazole rings.

Diazo compounds failed to form upon diazotizing the amines by standard procedure because the azo dyes formed instantly upon addition of the sodium nitrite; the coupling products of diazotized amines with non-diazotized are explainable by the singular activity of the benzene nuclei of aminopiazothioles (X) and (XI); therefore, the corresponding diazo compounds reacted further with smoothness when reaction was carried out in the presence of excess nitrous acid.

From the diazo compounds, according to the Sandmeyer reaction, 4-chloropiazothiole (XIX) and 5-chloropiazothiole (XX) were obtained:


(XIX)


(XX)

Absorption spectra in the near ultra-violet and visible ranges were studied for all piazothiole derivatives described in this work.

As can be seen from Fig. 1, for piazothiole itself, two very intense and monochromatic maxima (absorption bands) in the ultra-violet region at λ_{1max} = 200 mμ and λ_{2max} = 310 mμ are characteristic.

The presence of both maxima can be observed without exception for all derivatives of piazothiole.

The introduction of an amino group in the 4 or 5 position of the piazothiole molecule (Fig. 2) shifts the first maximum by 10-20 mμ toward the long waves, the second maximum remaining without evident change, and the third maximum appearing in the visible range, which determines the yellow color of aminopiazothiole. Acylation of the amino groups affects but very little the positions of the first two maxima for aminopiazothioles.

Introduction of a nitro group in position 4 or 5 (Fig. 3) shifts quite markedly both piazothiole maxima to the short wave range (by 40-50 mμ), and moreover, near the visible range there appears in both isomers a third maximum which determines the light-yellow color of the nitro derivatives. It is of interest to observe that the introduction of the sulfonic and chlorine groups has no evident effect upon the maxima positions (Fig. 1).

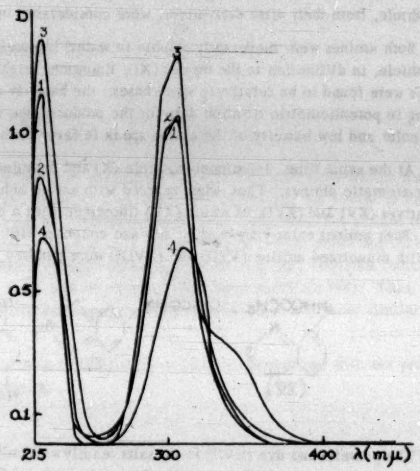


Fig. 1. Absorption spectra: 1) piazothiole; 2) piazothiole-4-sulfonic acid; 3) 4-chloropiazothiole; 4) 5-chloropiazothiole.

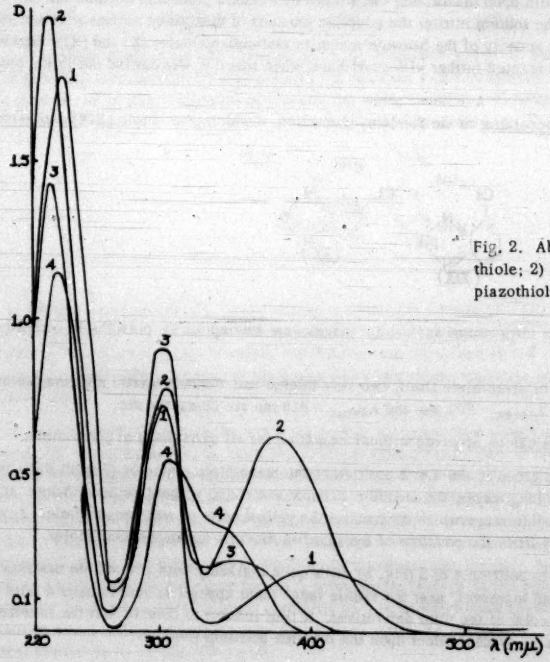


Fig. 2. Absorption spectra: 1) 4-aminopiazothiole; 2) 5-aminopiazothiole; 3) 4-acylaminopiazothiole; 4) 5-acylaminopiazothiole.

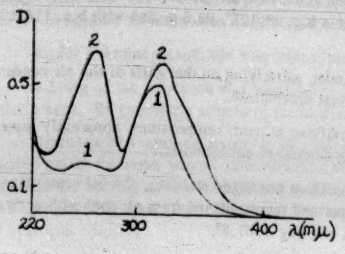


Fig. 3. Absorption spectra: 1) 4-nitropiazothiole; 2) 5-nitropiazothiole.

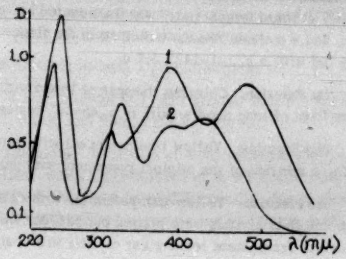


Fig. 4. Absorption spectra: 1) 4-amino-7-benzeneazothiole; 2) 5-amino-5-benzeneazopiazothiole.

The presence of two maxima which are specific for the piazothiole ring can also be found in both azo dyes: they are shifted by 10-40 mμ to the long wave length end; in addition, both dyes have two other maxima in the visible range which determine their colors (Fig. 4).

The experimental data given in this work confirm the accuracy of a quinoid formula for the piazothiole structure (III), at the same time demonstrating that the quinoid structure does not result in unsaturation, instability or increased reactivity of the compound.

EXPERIMENTAL

Sulfonation of piazothiole. 1 g of piazothiole and 15 g of 17% oleum (d 1.897) were introduced into a 50 ml flask, equipped with reflux condenser. The mixture was heated for 1 hour at 150°, cooled and diluted with 100 ml of water. The resulting solution was partially neutralized with 12 g of sodium bicarbonate and saturated with sodium chloride (7-8 g) with heating. After cooling, light-brown, lustrous needles precipitated. Yield was 1.36 g (78% calculating for the Na salt). The product was crystallized from alcohol. 0.93 g of a light-yellow substance with m.p. 385-390° resulted. Transparent rectangular platelets were visible under the microscope.

0.00333, 0.00691 g sub.: 0.336 ml N_2 (21°, 754 mm), 0.692 ml N_2 (21.5°, 754.5 mm). 0.1538, 0.1530 g sub.: 0.3004, 0.2960 g $BaSO_4$. Found %: N 11.62, 11.55; S 26.75, 26.57. $C_6H_3O_3N_2S_2Na$. Calculated %: N 11.75; S 26.87.

To determine the structure of the resulting compound, it was reduced to the corresponding diamine [11].

5 g of the sodium salt of piazothiolesulfonic acid, 20 ml of water and 3 ml of concentrated hydrochloric acid were placed in a 50 ml flask, and the mixture heated to complete dissolution. 10 g of zinc dust was added in small portions to the resulting solution. Reduction immediately started, accompanied by intense evolution of hydrogen chloride. 40 ml of concentrated hydrochloric acid was added to the decolorized solution. Colorless crystals of 1,2-phenylenediamine-3-sulfonic acid hydrochloride precipitated. The yield was 2.6 g (55% calculating on the basis of monohydrochloride). After recrystallization from water with activated charcoal, colorless needles, melting with decomposition at 276-278° resulted.

The resulting compound was converted to the benzimidazole derivative by heating in a sealed tube at 180° for 40 minutes 0.4 g of 1,2-phenylenediamine-3-sulfonic acid hydrochloride with 3 ml of 98% formic acid. There resulted a transparent pinkish solution, from which large pink prisms gradually precipitated. The solution was evaporated to dryness on a water bath. The pinkish precipitate was recrystallized several times from a small amount of water with activated charcoal. Lustrous, colorless platelets in the form of parallelograms were obtained, with a m.p. of 360-363°. The yield of pure product was 0.1 g. A sample mixed with benzimidazole-5-sulfonic acid melted at 247-252° (i.e., gave depression).

0.1244 g sub.: 15.7 ml N_2 (25°, 755 mm). 0.1632 g sub.: 0.1891 g $BaSO_4$. Found %: N 14.36; S 15.88. $C_7H_5O_3N_2S$. Calculated %: N 14.14; S 16.16.

Chlorination of piazothiole. 43.2 g of piazothiole and 1 g of iron filings were placed in a flask, 80 ml in volume, provided with thermometer and tube for chlorine inlet and outlet. The flask was placed in a water bath with water temperature at 60°. A strong stream of chlorine was passed through the melt, and the flask weighed every 15 minutes. Chlorination was terminated when the weight increase amounted to 10.8 g, corresponding to complete

conversion of the given amount of piazothiole to the monochloroderivative. The resulting brown oil which did not solidify at room temperature, was fractionated by vacuum distillation at 14-22 mm. There were collected 3 fractions, and a resinous residue remained in the flask: 1st fraction with a b.p. 98-105°, 23.6 g; 2nd with b.p. 114-130°, 92 g; 3rd with b.p. 131-140°, 3.2 g.

1st Fraction: Colorless transparent liquid with characteristic odor, solidifying on the walls of the air condenser in the form of long needles with m.p. 43-44°, representing the original piazothiole.

2nd Fraction: Yellow transparent oil with sharp odor, not solidifying at room temperature, apparently representing a mixture of the original compound with products of varying degrees of chlorination.

3rd Fraction: Yellow transparent oil with characteristic odor. Upon prolonged standing, the oil crystallized. Large colorless crystals were pressed out between sheets of filter paper and recrystallized from alcohol with activated charcoal. Transparent rectangular crystals with sharp odor resulted, melting at 57.5°.

A sample mixed with 4-chloro- and with 5-chloropiazothiole gave depression.

0.1152, 0.1206 g sub.: 13.6 ml N_2 (24°, 756 mm). 714.4 ml N_2 (23°, 755 mm). 0.02843 g sub.: 5.460 ml $Hg(NO_3)_2$ (T 1.847). Found %: N 13.60, 13.71; Cl 34.45. $C_6H_2Cl_2N_2S$. Calculated %: N 13.65; Cl 34.66.

5-Nitropiazothiole synthesis. 27 g of 1-nitro-3,4-diaminobenzene, 250 ml of dry xylene and 40 ml (67 g, 60% excess) thionyl chloride were placed in a 0.5 liter, two-necked flask equipped with reflux condenser, calcium chloride tube and thermometer. The mixture was heated for 6 hours on an oil bath, in such manner as to boil slowly. At 94° an intense evolution of hydrogen chloride had already begun, and the reaction mixture acquired a red-brown color, the temperature gradually rose and became constant at 125°, and at the end of the reaction reached 127°. A small volume of water was added to the reaction mixture to decompose the excess thionyl chloride, and the 5-nitropiazothiole distilled out with superheated steam. Distillation proceeded slowly: for 0.4 liter of distillate, 2 g of the product distilled out. 24.5 g (75.5%) of light yellow substance, with m.p. 127°, resulted.

Experimental data resulting from the experiments carried out under various conditions are given in the Table.

Expt. No.	Amount				Type of solvent	Heating time (hrs)	Temperature	Yield (%)
	1-nitro-3,4-diaminobenzene (g)	thionyl chloride (g)	(%)	solvent (ml)				
1	4	9.3	150	30	Toluene	8	105°	34
2	4	9.3	150	30	"	1.5	130	52
3	4	10.9	180	30	"	1.5	120	43
4	10	23.4	150	90	Xylene	6	125-127	72.5
5	20	46.8	150	120	"	6	125-127	76.4
6	27	67	160	250	"	6	125-127	75.5

Note: Experiments 2 and 3 were carried out in sealed tubes.

5-Nitropiazothiole is a light-yellow compound with characteristic odor. After recrystallization from alcohol with activated charcoal, flat platelets were clearly evident under the microscope, in the form of parallelograms with m.p. 128°.

5-Nitropiazothiole is insoluble in water, poorly soluble in the cold in alcohol, ether, benzene, toluene and carbon tetrachloride.

Synthesis of 5-aminopiazothiole by reduction of 5-nitropiazothiole. 30 g of pig iron shavings and 250 ml of water were introduced into a two-necked, 0.5 liter flask, equipped with reflux condenser and stirrer. The stirrer was turned on and the mixture heated to boiling on an oil bath. 5 ml of 97% acetic acid was added to the boiling liquid, and after a certain period of time, 10 g of 5-nitropiazothiole was poured in through a funnel. The mixture was boiled for 20 minutes. The hot, red-brown reaction mixture was filtered with suction from the residue. The residue was washed carefully with hot water (200-250 ml) and the wash waters were added to the main filtrate. (It was convenient to use the wash water residue in the following tests.)

The turbid, yellow filtrate, smelling strongly of amine was cooled rapidly and from it precipitated the amine in the form of yellow needles. They were separated and dried in a desiccator. 5 g (59.5%) of yellow-brown substance with m.p. 113-114° resulted. The filtrate was acidified with hydrochloric acid, evaporated to 50 ml and extracted with ether. 1.2 g of yellow-brown substance, with m.p. 113° resulted. The total yield of product was 6.2 g (74.5%).

After recrystallization from water with activated charcoal, 5-aminopiazothiole resulted in the form of light-yellow needles with m.p. 117°. 5-Aminopiazothiole was poorly soluble in cold water, more so in hot water, and dissolved readily in organic solvents, also dissolving in moderately concentrated solutions of hydrochloric acid.

K_b for 5-aminopiazothiole was determined by potentiometric titration with a glass electrode.

0.100 g of the substance was dissolved in 50 ml of water-alcohol mixture (3:1) and titrated with 0.1 N hydrochloric acid. By geometric structure, the half-way point, A, was found, and from it the K_b (Fig. 5).

Synthesis of 4-aminopiazothiole by reduction of 4-nitropiazothiole. Reduction of 4-nitropiazothiole was carried out in the same way as with reduction of 5-nitropiazothiole: using pig iron shavings in 2% acetic acid solution, but the boiling time was shortened to 5 minutes, since otherwise the yield dropped drastically, due to start of a side reaction involving reduction of 4-nitropiazothiole to triaminobenzene, accompanied by intense evolution of hydrogen chloride.

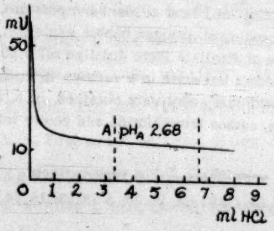


Fig. 5. Potentiometric titration of 5-aminopiazothiole.

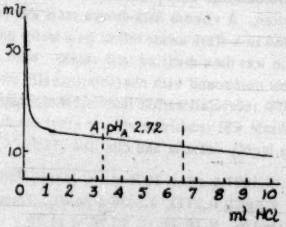


Fig. 6. Potentiometric titration of 4-aminopiazothiole.

Total yield was 72%. After rectystallization from water with activated charcoal, beautiful long, green-yellow needles of 4-aminopiazothiole resulted, with m.p. 68°.

4-Aminopiazothiole was readily soluble in organic solvents, dissolving somewhat less so in water than 5-aminopiazothiole; also soluble in hydrochloric acid solution of moderate concentration.

K_b for 4-aminopiazothiole was determined by the method of potentiometric titration.

0.101 g of the substance was dissolved in 50 ml of water-alcohol mixture (3:1) and titrated with 0.1 N hydrochloric acid solution. The half-way point, A, was found by geometry (Fig. 6).

Synthesis of 4-acetylaminopiazothiole. 2.5 g of 4-aminopiazothiole and 7 g of acetic anhydride were introduced into a 50 ml flask equipped with reflux condenser. The flask was heated for 0.5 hour on a boiling water bath. Its contents were then transferred to a beaker. The flask was rinsed, wash water being added to the main mixture in such a manner than the total volume of liquid did not exceed 30-40 ml. The liquid was heated to boiling and neutralized with ammonia. Light-yellow scales of the acetyl derivative precipitated. After cooling, they were separated and washed with a small amount of water. Yield was 3.1 g (97%). M.p. was 150-151°. The substance was recrystallized from water with activated charcoal. Large, lustrous, mica-resembling, transparent, light-yellow, rectangular platelets with m.p. 152.5° resulted.

The compound was soluble in alcohol, ether, benzene, poorly soluble in toluene, soluble to some extent in cold water, and quite readily soluble in hot water.

Under the action of ultra-violet radiation, 4-acetylaminopiazothiole shone brightly with a blue glow.

0.0970, 0.0992 g sub.: 18.7 ml N_2 (21.5°, 755 mm), 18.8 ml N_2 (21°, 755 mm). 0.1111, 0.1158 g sub.: 0.1330, 0.1427 g $BaSO_4$. Found %: N 22.19, 21.85; S 16.43, 16.90. $C_8H_7ON_3S$. Calculated %: N 21.75; S 16.60.

Coupling of 4-aminopiazothiole with diazobenzene. 2 g of a solution of sodium nitrite in 10 ml of water was added up to the point of positive reaction with starch-iodide paper, to a solution of 2 g of freshly-distilled aniline in 15 ml of 20% hydrochloric acid, at 0°. 3 g of 4-aminopiazothiole was dissolved in 40 ml of 25% hydrochloric acid. With gradual mixing, the amine solution was added to the diazobenzene solution at 0-2°. Almost immediately, the liquid acquired an intense dark-red color. Sodium acetate was added to the mixture to the disappearance of an acid reaction to Congo red. After 2-3 hours, the dark red viscous mass was separated and washed with water. The azo dye remained on the filter as dark clots, or resinous lumps. The substance was dried at 80-90° and ground in a mortar. 4.5 g (89%), calculating on the basis of azo dye, resulted of dark-brown powder, m.p. 178-185°.

To obtain chemically-pure product, it was recrystallized from alcohol with activated charcoal. A small amount of dark-red crystals was obtained, in the form of truncated tetrahedral prisms. M.p. 198-199°. A larger amount of quite pure compound can be obtained by reprecipitation from alcohol with hot water. The product is soluble in alcohol, acetone, glacial acetic acid, insoluble in water, dissolving in hydrochloric acid with a deepening of color. The orange-red azo dye base can be precipitated from hydrochloride solution by ammonia.

0.0511, 0.0803 g sub.: 13.3 ml N_2 (22°, 756 mm), 19.2 ml N_2 (22.5°, 756 mm). 0.0960, 0.1014 g sub.: 0.0852, 0.0941 g $BaSO_4$. Found %: N 27.71, 27.47; S 12.17, 12.72. $C_{12}H_9N_5S$. Calculated %: N 27.43; S 12.56.

Synthesis of 4-chloropiazothiole. 0.6 g of sodium nitrite (30% excess) in 10 ml of cold water solution was added to 25 ml of concentrated hydrochloric acid, precooled to 0°, 1 g of a solution of aminopiazothiole in 15 ml of concentrated hydrochloric acid was immediately added to the mixture. There resulted a light-red transparent diazopiazothiole solution. The excess nitric acid was removed by addition of urea to the point of negative reaction to starch-iodide paper. The diazopiazothiole solution was then added slowly, with stirring, to a solution of cuprous chloride in hydrochloric acid precooled to 0°, obtained by reduction of 6 g of copper sulfate, 30 ml of 37% sodium bisulfate solution. A viscous dark-brown mass was formed. After standing for 1 hour at room temperature, the solution was heated in a flask under reflux on a water bath at 60-80° to cessation of nitrogen bubble evolution. The reaction mixture was then distilled with steam. With the very first drops of distillate there distilled off 0.20 g (18%) of light-yellow compound with characteristically strong odor. The product was dried in a vacuum desiccator. M.p. 53.5-54°. After recrystallization from alcohol, light-yellow needles with sharp odor were obtained, m.p. 55°. 4-Chloropiazothiole was readily soluble in ethyl alcohol, ether, benzene, carbon tetrachloride, and poorly soluble in water. It was highly volatile and distilled readily with steam.

0.0964, 0.1037 g sub.: 13.8 ml N_2 (24.5°, 755 mm), 15.0 ml N_2 (24°, 755 mm). 0.1266, 0.1529 g sub.: 0.1078, 0.1297 g AgCl; 0.1711, 0.2088 g $BaSO_4$. Found %: N 16.32, 16.50; Cl 21.09, 21.00; S 18.53, 18.74. $C_8H_3N_2SCl$. Calculated %: N 16.42; Cl 20.78; S 18.79.

Synthesis of 5-acetylaminopiazothiole. 5-Acetylaminopiazothiole was synthesized under conditions similar to the synthesis of 4-acetylaminopiazothiole. The yield was 91%. Light-yellow, lustrous scales with m.p. 190° After recrystallization from water with activated charcoal, light yellow needles resulted with m.p. 190°. The substance dissolved in hot water and alcohol, was poorly soluble in ether, benzene and carbon tetrachloride.

0.0902, 0.0840 g sub.: 17.2 ml N_2 (21°, 755 mm). 16.3 ml N_2 (23°, 754 mm). 0.1053, 0.1139 g sub.: 0.1252, 0.1374 g $BaSO_4$. Found %: N 21.99, 22.20; S 16.32, 16.56. $C_5H_7ON_2S$. Calculated %: N 21.75; S 16.60.

Coupling of 5-aminopiazothiole with diazobenzene. Reaction was carried out under conditions similar to those for 4-aminopiazothiole coupling. An orange-red dye resulted in 71% yield. M.p. was 205-206°. The product was insoluble in water, soluble in alcohol, acetone, glacial acetic acid, giving colorations ranging from light orange to bright red. Hydrochloric had no action upon it. After recrystallizing from alcohol with activated charcoal, beautiful lustrous, red crystals were obtained. Under low power of the microscope were seen large orange-red rectangular platelets. M.p. was 225-227°.

0.0840, 0.0798 g sub.: 20.2 ml N_2 (23.5°, 754 mm); 19.3 ml N_2 (24°, 754 mm); 0.1351, 0.1382 g sub.: 0.1223, 0.1271 g $BaSO_4$. Found %: N 27.46, 27.57; S 12.43, 12.62. $C_{12}H_9N_5S$. Calculated %: N 27.43; S 12.56.

Synthesis of 5-chloropiazothiole. 5-Chloropiazothiole was obtained in a manner similar to that for 4-chloropiazothiole, according to the Sandmeyer reaction under the same conditions. Yield was 41%. Colorless needles with m.p. 56-57°. Silvery needles were obtained after recrystallization from alcohol with activated charcoal, melting at 57°. 5-Chloropiazothiole has a very sharp odor, is volatile and considerably hygroscopic. Readily soluble in ether, alcohol, benzene, carbon tetrachloride, and insoluble in water.

0.0919, 0.1121 g sub.: 13.3 ml N_2 (25°, 755 mm), 15.9 ml N_2 (24°, 755 mm). 0.1424, 0.1562 g sub.: 0.1182, 0.1318 g AgCl; 0.1923, 0.2120 g $BaSO_4$. Found %: N 16.47, 16.17; Cl 20.54, 20.87; S 18.52, 18.63. $C_8H_3N_2SCl$. Calculated %: N 16.42; Cl 20.78; S 18.79.

Spectroscopy

Absorption spectra for piazothiole and its derivatives were taken on a spectrophotometer SF-4. Measurements were carried out in water solutions, excluding the two azo dyes. Spectra of the latter were taken in alcoholic solution. Measurements were carried out in the long wave length range: 215-600 mμ at 10 mμ intervals.

SUMMARY

1. A study of the chemical properties of piazothiole and certain of its simplest derivatives has confirmed that this compound possesses a quinoid structure.

2. At the same time, piazothiole does not possess unsaturation and reactivity toward addition reactions which are characteristic for quinones. Characteristic of it are substitution reactions proceeding under the influence of electrophilic reagents at position 4 (7).

3. The 4- and 5-aminopiazothiole isomers possess all the properties of normal aromatic amines, displaying increased tendency to substitution reactions in the nucleus.

4. Two characteristic absorption bands in the near ultraviolet region have been observed in the absorption spectra for piazothiole and all of its derivatives which were studied.

LITERATURE CITED

[1] O. Hinsberg, Ber., 22, 2895 (1889); German Patent 14191; Frdl., 2, 534.

[2] Michaelis, Ann., 274, 262 (1889).

[3] Luzzati, Acta Crist., 4, 193 (1951).

[4] L. S. Efros, J. Gen. Chem., 22, 1008 (1952).*

[5] K. Fries, Ann., 454, 131 (1927), 389, 305 (1912).

[6] K. Fries, Ann, 454, 121 (1927); L. Fieser, Organic Chemistry 669, 690 (1950).

[7] L. S. Efros and R. M. Levit, J. Gen. Chem., 23, 1552 (1953).**

[8] A. M. Khaletsky and V. G. Pesin, J. Gen. Chem., 20,1914 (1950).***

[9] L. S. Efros, J. Gen. Chem., 23, 842 (1953).****

[10] A. M. Khaletsky and V. G. Pesin, J. Gen. Chem., 24, 133 (1954).*****

[11] G. C. Chakravarti, Quart. J. Ind. Chem. Soc., 2, 71 (1925).

Received May 18, 1954

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* See Consultants Bureau Translation, page 1063.
** See Consultants Bureau Translation, page 1629.
*** See Consultants Bureau Translation, page 1981.
**** See Consultants Bureau Translation, page 881.
***** See Consultants Bureau Translation, page 131.

SYNTHESIS AND POLYMERIZATION OF ACRYLIC AND METHACRYLIC ACID ESTERS WITH NITROPHENOLS

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Trinitrophenyl esters are described in the literature [1], obtained from acrylic and methacrylic acid esters with nitrophenols, which, when heated with benzoyl peroxide, lead to polymerization. Soon after completion of the present work (1951), data were published concerning synthesis and polymerization of 2- and 4-nitrophenylmethacrylates [2].

For the synthesis of nitrophenyl esters, the authors utilized the reaction of corresponding chloroanhydrides with nitrophenols in inert solvent and in the presence of anhydrous sodium carbonate [3]:

$$ArOH + CH_2=CRCOCl \longrightarrow ArOOCCR=CH_2 + HCl$$

$$HCl + Na_2CO_3 \longrightarrow NaHCO_3 + NaCl$$

Without sodium carbonate, or other substances to tie up the hydrogen chloride, as was indicated in the patent [3], the latter can add at the double bond. Cuprous chloride in the amount of 2-3% of nitrophenol weight, was used as the inhibitor of polymerization during the ester synthesis.

While this reaction proceeded in the cold with phenol, it required heating at 60-80° for nitrophenols. It was observed that for the same time and temperature of reaction, the ester yields decreased in the order: phenol → → m-nitro → p-nitro → o-nitro → 2,4-dinitrophenol, where the introduction of each additional nitro group has particularly strong effect. Hence, reactivity of phenols with respect to esterification follows the same order.

Anhydrous dichloroethane, benzene and carbon tetrachloride were tested by the authors for solvent use. The best results were obtained with dichloroethane, which dissolves nitrophenols and esters readily, whereas, with the latter two solvents, reaction proceeds under partially heterogeneous conditions. It is possible that the specific effect of dichloroethane is due to its being the strongest dissociating solvent.

It should be mentioned that the synthetic method used by the authors gives good ester yields, higher than were indicated in works by the American authors [2].

Analysis of the resulting esters was carried out by hydrolysis with a water-dioxane solution of alkali, excess of which was removed by titration. The hydrolyzed sample was treated in the usual manner with bromide-bromate solution. From the results obtained, the ester and bromine numbers were calculated. The ester content of the resulting products, calculating according to hydrolytic data, amounted to 92.3-99.0%, and in double bond content, 91.9-99.9%. In actuality the purity of the products was considerably higher, inasmuch as a majority of them were crystalline compounds which had been repeatedly recrystallized. Depressed analytical results are explicable only by insufficient accuracy of the analysis, since nitrophenols themselves react also with both alkali and bromine, for which appropriate corrections had to be made in the analytical data.

Of the products obtained by the authors, the o-nitrophenyl esters were found to be almost colorless liquids, the m- and p-nitrophenyl esters colorless crystalline compounds, and the 2,4-dinitrophenyl esters crystalline compounds of yellowish color. Some of their constants are listed in Table 1.

It is of interest to note that the methacrylic acid esters melted at higher temperatures than the corresponding acrylates.

All of the esters which were synthesized could be polymerized at elevated temperature in the presence of peroxides. At 70° with 0.5% benzoyl peroxide, polymerization proceeded very slowly, and after 20-hour heating, the resulting polymers were still not solid. At 80° and 2% benzoyl peroxide, polymerization went much more rapidly – after 2 hours, considerable solidification had occurred, and after 4-6 hours, there were obtained polymers which were quite solid. p-Nitrophenylmethacrylate, melting at higher temperature, polymerized at 120° with the same quantity of peroxide.

All polymers obtained by the authors were in the form of solid, transparent substances of yellowish color. They were insoluble in benzene and dichloroethane. Acetone dissolved only the dinitrophenyl ester polymers. The best solvent was found to be nitrobenzene, which had to be used for determining the molecular weight of the polymers by viscosity. Certain properties of the polymers are given in Table 2.

TABLE 1

No.	Name	Temperature		d_4^{20}
		Melting	Boiling	
1	o-Nitrophenylacrylate	–	128-130° (2.5 mm)	1.263
2	m-Nitrophenylacrylate	34-35°	–	–
3	p-Nitrophenylacrylate	59-60	–	–
4	2,4-Dinitrophenylacrylate	44-45	–	–
5	o-Nitrophenylmethacrylate	–	134-136 (2 mm)	1.226
6	m-Nitrophenylmethacrylate	58-59	–	–
7	p-Nitrophenylmethacrylate	93-94	–	–
8	2,4-Dinitrophenylmethacrylate	58-69	–	–

Of all the polymers, the most unusual was found to be poly-m-nitrophenylmethacrylate, which decomposed upon heating, without melting, and did not dissolve in any of the solvents tried.

TABLE 2

No.	Polymer	Melting point	Molecular weight
1	o-Nitrophenylacrylate	80-100°	56,500
2	m-Nitrophenylacrylate	75-95	71,800
3	p-Nitrophenylacrylate	75-100	49,800
4	2,4-Dinitrophenylacrylate	68-94	39,300
5	o-Nitrophenylmethacrylate	130-170	80,000
6	m-Nitrophenylmethacrylate	Decomposes	–
7	p-Nitrophenylmethacrylate	124-145	45,200
8	2,4-Dinitrophenylmethacrylate	110-127	66,900

Since formation of a three-dimensional structure for the given case is excluded, the authors assume that this polymer has a high molecular weight and melting point, because of which it is the least soluble, and decomposes before it reaches its melting point.

As can be seen from Table 2, the melting points of the polymers were quite low, especially so for the acrylates. The highest molecular weights were obtained for the m-nitrophenyl esters (poly-m-nitrophenylmethacrylate almost insoluble), then the o-nitro, p-nitro-, and dinitrophenyl esters (p-nitrophenylmethacrylate polymerized at higher temperature, and the molecular weight of the polymer obtained was, therefore, less).

EXPERIMENTAL

Synthesis of the esters. The apparatus for synthesis of the esters consisted of a three-necked flask with stirrer, reflux condenser and dropping funnel. To avoid entrance of moisture, the stirrer was equipped with mercury seal, and the condenser and dropping funnel were protected with calcium chloride tubes.

The flask was immersed in a water bath and into the former was charged 16 g of anhydrous sodium carbonate, finely-powdered, 0.5 g of cuprous chloride, 0.1 mole of nitrophenol and 10-15 ml of anhydrous solvent. 0.11 mole of chloroanhydride (10% excess in relation to the nitrophenol) was added from a dropping funnel over a period of 5-10 minutes with vigorous stirring, the water bath being heated rapidly to 60° and kept at this temperature for 2-3 hours. After cooling, the precipitated inorganic salts were separated, washed with solvent and the filtrate treated with aqueous sodium carbonate solution to the point of neutrality. The solvent was then distilled off in vacuo. In the case of m- and p-nitro- and dinitro-phenyl esters, the product was crystallized after distilling off the solvent. The crystals were separated from the mother liquor and recrystallized repeatedly from methyl alcohol until a constant melting point was reached. In the case of o-nitrophenyl esters, liquids under normal conditions, the product, after distilling off the solvent, was distilled in vacuo with sampling of a narrow fraction (Table 1).

The theoretical yields of esters (in parenthesis are given the reaction conditions and solvents used) (in %):

o-Nitrophenylacrylate	62	(2 hours at 60° in dichloroethane)
m-Nitrophenylacrylate	46.6	(2 hours at 60° in CCl_4).
p-Nitrophenylacrylate	37	(2 hours at 60° in CCl_4)
2,4-Dinitrophenylacrylate	36	(2.5 hours at 80° in CCl_4)
o-Nitrophenylmetacrylate	47.5	(3 hours at 60° in benzene)
m-Nitrophenylmetacrylate	52	(2.5 hours at 60° in benzene)
p-Nitrophenylmetacrylate	42	(2 hours at 60° in benzene)
p-Nitrophenylmetacrylate	87	(2.5 hours at 60° in dichloroethane)
2,4-Dinitrophenylmetacrylate	59.5	(2 hours at 60° in dichloroethane)

Polymerization and investigation of the polymers. Polymerization of the esters was carried out in test tubes, in which the pure ester, amounting to 2-3 g was placed with benzoyl peroxide. The test tube was kept for the required time in a thermostat at a temperature regulated within an accuracy of ± 0.2°. The resulting polymers were not further purified.

The melting points of the polymers were determined in a capillary by the usual procedure. The lower range of melting point corresponded to appearance of droplets, the upper limit to the formation of a clear meniscus of melted polymer.

Molecular weights of the polymers were determined by the viscosity of 0.5% solution in nitrobenzene. Inasmuch as the K_T value of the Staudinger equation for nitrobenzene solutions is not known, the authors determined it by means of polyphenylacrylate, of known molecular weight (32,400) by measuring the viscosity of its 0.5% solution in nitrobenzene:

$$K_T = \frac{\eta_{sp}}{M \cdot c} = \frac{0.0595}{32,400 \cdot 0.0278} = 0.66 \cdot 10^{-4}.$$

SUMMARY

1. Acrylic and metacrylic esters of o-nitro-, p-nitro- and 2,4-dinitrophenols have been synthesized and characterized.

2. Polymers of these esters have been synthesized and their melting points and molecular weights determined.

LITERATURE CITED

[1] H. Bruson, G. Butler, U. S. Patent 2407131; Chem. Abs., 41, 288 (1947).

[2] S. Patav, M. Benton, M. Reichmann, J. Am. Chem. Soc., 74, 845 (1952).

[3] German Patent 570955 (1933).

Received May 22, 1954

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